Virology 1

Basic virology

Properties differentiating viruses from other organisms

Smallest infectious org.

(10-300 nm)

Either DNA or RNA

Obligate IC org.

Have **no ribosomes**

No metabolic activity EC

Enters host cells

Introduces DNA or RNA

Directs host cell transcription &translation

New copies of viral genes & proteins

New viral particles (virions)

Structure of virus

Virion (intact virus particle) consists of

Nucleocapsid

basic structure of viruses

Genome

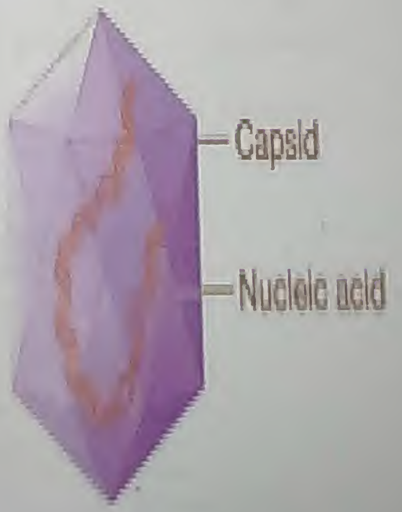
Nucleic acid core

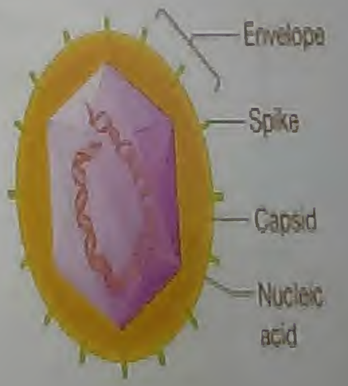
Capsid

Protein coat

Envelope

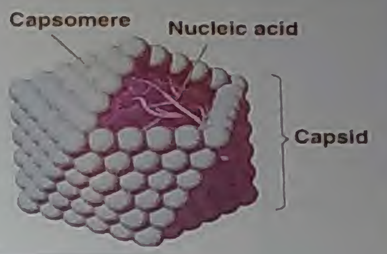
In **some** viruses





(b) Enveloped virus

I - Capsid (protein coat)

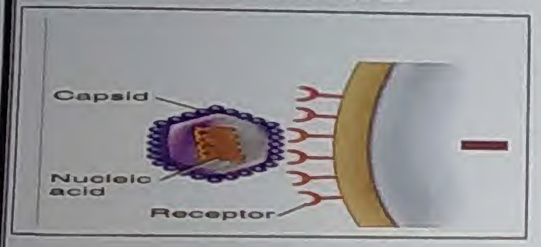


A-Structure

- Encloses genome
- Formed of protein subunits cd ***capsomeres***

B-Functions

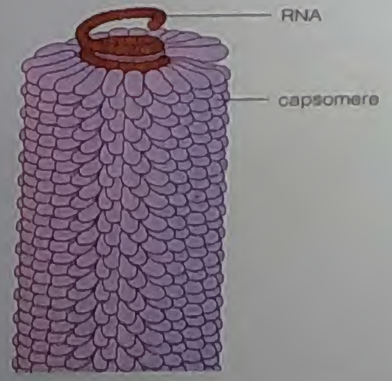
- **Protection** of nucleic acid from ***nucleases***
- **Attachment** to host cells Via ***specific receptors*** (in non enveloped viruses)
- **Shape** ***Symmetry*** of virus
- **Antigenic**
  - Induce ***neutralizing Abs***
  - ⊕ ***CTLs*** → Kill VICs



Shape (Symmetry) of viruses

According to **arrangement of capsomeres** in capsid

- **Helical**
  - Hollow ***coil***
  - Myxo viruses
- **Icosahedral (cubic)**
  - *20 triangles* ***Outline of sphere***
  - Most viruses
- **Sperm like**
  - ***Head & tail***
  - Bacterio-phages
- **Complex**
  - ***More complicated***
  - Pox virus



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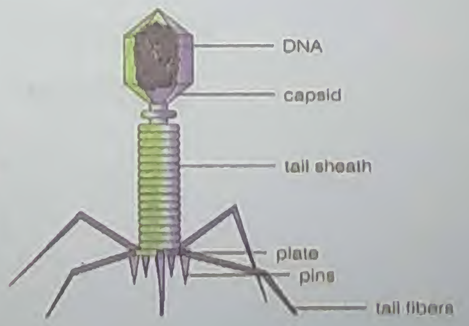
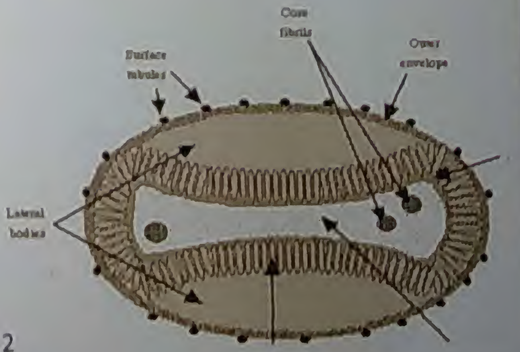




II – Envelope

Liporotein membrane surrounding some viruses

Lipid part

- *Derived from* **host CM or NM** by **budding**
- Confers **instability on virus**: Enveloped V are **more sensitive** to heat & detergents (alcohol and ether)
- **Disruption**: Virus killing

Glycoprotein part

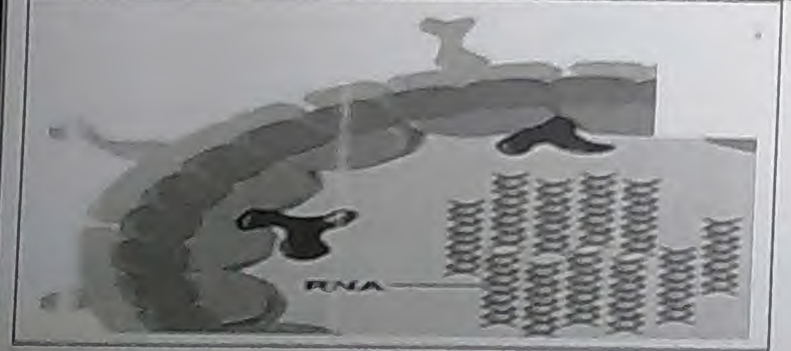
Virus specific e.g Haemagglutinin (HA)

- **Attach** to specific receptors on host cells
- **Ag** → Humoral IR

III-Genome (Nucleic acid core)

A-Classification

RNA viruses				DNA viruses	
All are SS except **Reoviruses** (Rota V)	***All are non segmented*** except: ♦ Bunya ♦ Rota V ♦ Influenza V	***Types*** +ve sense: RNA is ***infectious*** ⬇ acts as mRNA in infected cell	-ve sense: RNA ***isn't infectious*** ⬇ Transcription by viral RNA polymerase → mRNA	***All are DS*** except **Parvo viruses**	***All are non segmented***



B-Functions

Infectivity

Viral replication

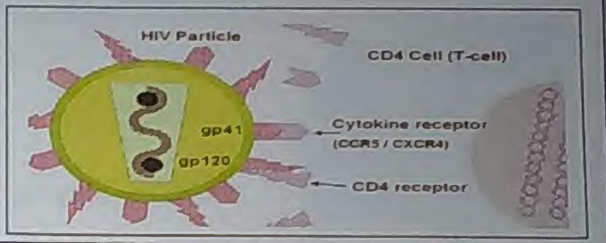
Viruses are metabolically ***inert EC***

↓

Obligate IC

↓

Replicate only inside living cells



1-Attachment

By viral proteins (on coat or envelope)
to ***specific*** host cell ***receptors***

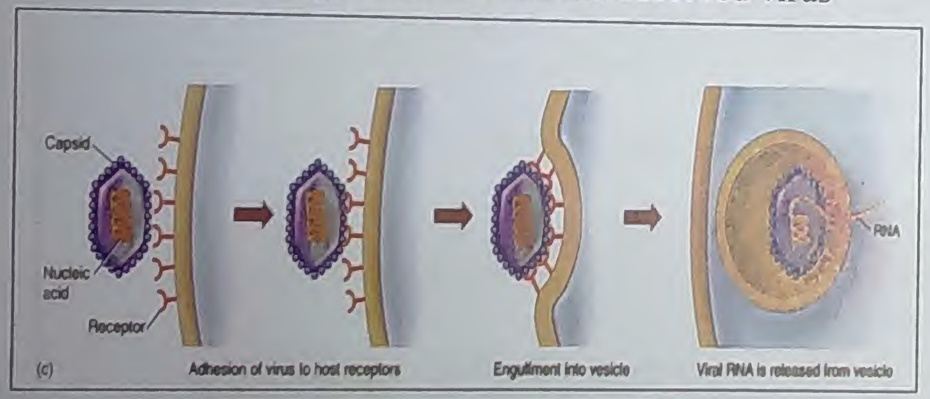
Example

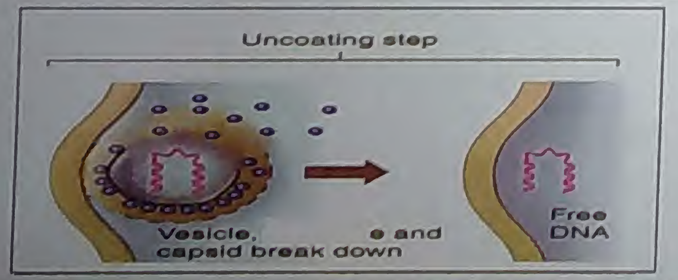
GP 120 on HIV attaches to **CD4** (receptor on T cells)

2-Penetration

Endocytosis (in **non enveloped** V)

CM invaginates around the adsorbed virus



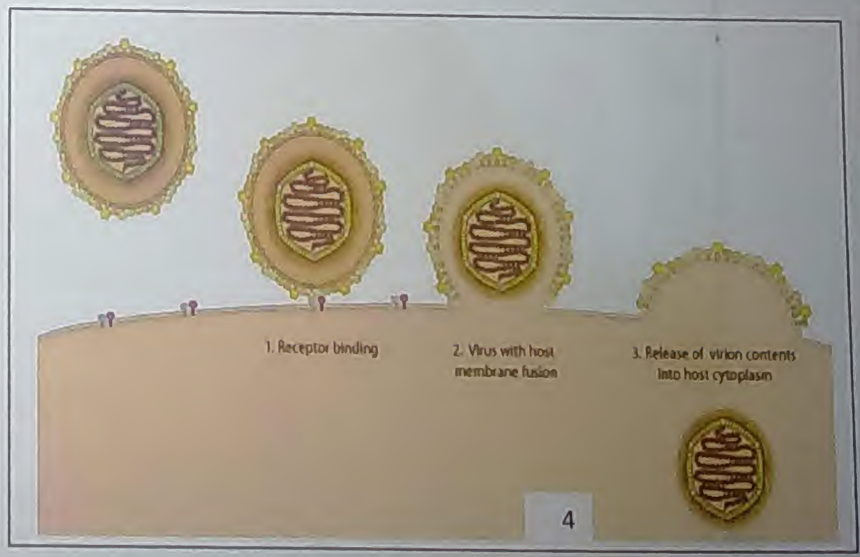


Fusion (in **enveloped** V)

Between envelope & host CM

↓

Naked nucleocapsid is released into cytoplasm



3-Uncoating

Host cell ***lysosymes***

remove viral capsid

4- Synthesis

Called eclipse : no viral particles are detected in host cell

Transcription

- **-ve sense**

Production of viral mRNA (by VRP)

(Using viral genome as template)

- **+ve sense**

– Genome itself acts as mRNA

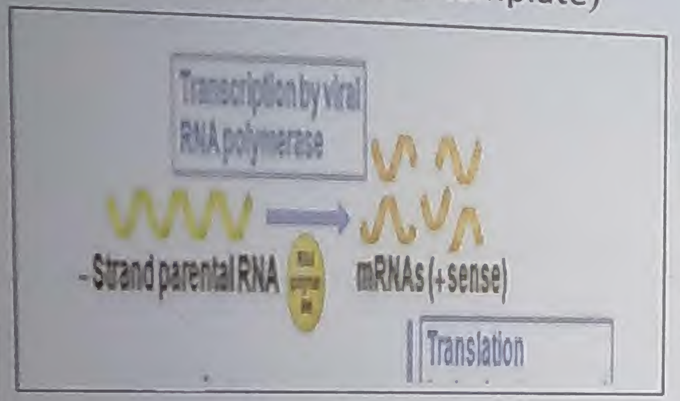
Translation

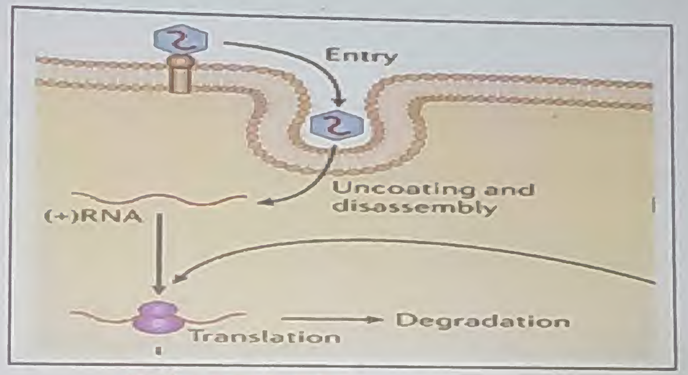
mRNA attaches to host ribosomes

⬇

Directs synthesis of viral proteins

Replication of nucleic acids



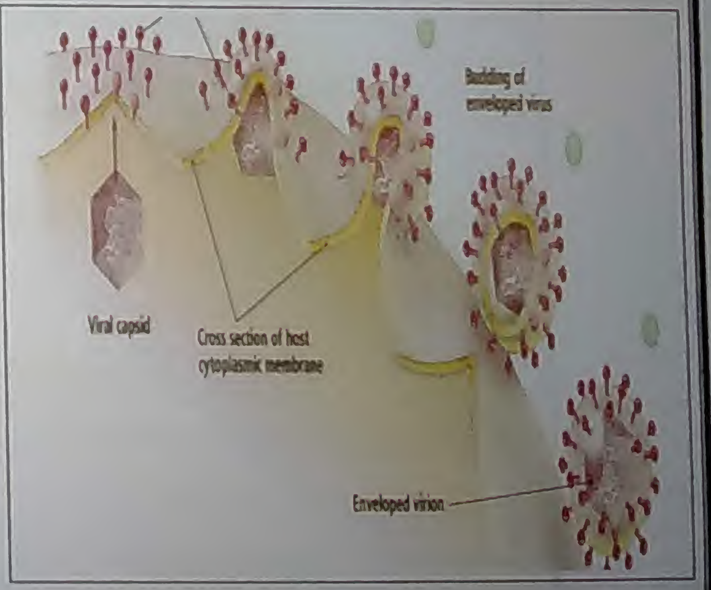


5-Assembly

New nucleic acids & structural proteins assemble

⬇

new virus progeny



6-Release

Rupture of cell

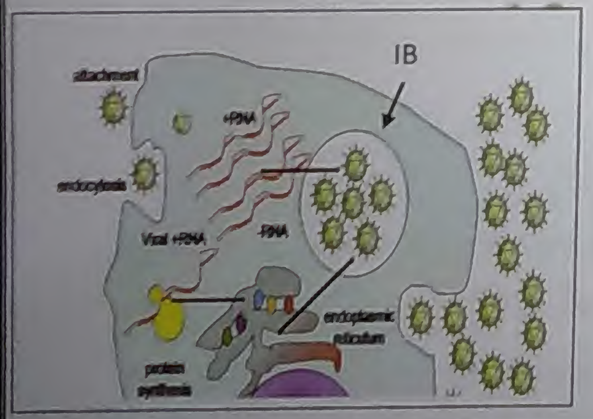
(cytolysis)

Non enveloped viruses

Budding

(gradual extrusion through CM)

Enveloped viruses



Steps of viral pathogenesis

Is the interaction of virus & host factors → ds production

1 - Routes of entry (transmission)

Horizontal

- Inhalation
- Ingestion
- Sexual
- *Inoculation*
  - ♦ Abraisions ♦ Injections
  - ♦ Bite of vector or animal ♦ Transfusion

Vertical (from mother to baby)

- Placenta
- Birth canal
- Breast feeding

2 - Local or 1ry replication

Viruses usually replicate at **the 1ry site of entry**

Some viruses ***only produce ds at site of entry*** on spreading locally over epithelial surfaces

With no

Invasion of underlying tissues ↔ *Spread* to distant sites

Examples

Influenza V → **RTI** ↔ Rota V → **GIT**

3 -Viral spread to target organs & cell tropism

a.Many viruses (after 1ry replication) produce ds at sites distant from site of entry

Routes of spread	**Example**
Blood (viremia) or lymphatics ↔ *Neuronal spread (rare)* e.g rabies	**Enteroviruses** enter through GIT(1ry replication) ↓ Spread ***CNS ds***

b.Mechanism of tropism (affinity to specific body tissues)

Presence of specific receptors	**Presence of proteolytic enzymes**	**Local temperature,pH&O_2 tension**
Polio V infects **nerve** cells ↔ *HIV* infects cells with **CD4**	Cleave envelope glycoprotein ***Paramyxoviruses*** become infectious	↓ temp.&↑O_2 tension of upper RT Multiplication of ***Rhinoviruses***

Types of viral diseases

	Localized ds	Systemic ds
1-Characters	Viruses invade only tissues **adjacent to site of entry** ⬇ **(no** viremia)	Viruses spread ⬇ ***Viremia*** → ***invades*** *many tissues & organs*
2-IP	**Short**	***Long***
3-Immunity	**Short** (transient)	***Long lasting***

4 - Effect of the virus on host cells

Cell death : cytopathic effect (CPE)

Etiology

Viral replication ↔ *CTLs* or NK cells

Effects

Cell injury ⬇

Lesions & dysfunction(symptoms&signs) in affected organs

Some tissues regenerate e.g intestinal epithelium

Others don't e.g brain

Cell transformation

Cell becomes malignant

(not killed)

5 - Host immune response & recovery from infection

Innate immunity

Adaptive immunity

Cell mediated ↔ Humoral

NB Viral classification

According to genome

DNA viruses

Enveloped ↔ Non enveloped

RNA viruses

Enveloped ↔ Non enveloped

According to host

i.Human
ii.Animal
iii.Arthropod
iv.Plants

According to ds

i.Respiratory viruses
ii.Enteric viruses
iii.Hepatitis viruses

6 - Fate of the virus after clinical recovery

Complete resolution

Viruses are

completely eliminated

from the body

↓

Viral clearance

Persistent viral infection

Chronic infection

V.persists in **1ry target**

↓

Slow replication

↓

Mild or no symptoms &pt is infectious

↓

Viral markers **are detected**

e.g **HBV** in liver

Latent infection

V.persists ***away from 1ry target***

↓

No replication (***occult***)

↓

No symptoms & pt isn't infectious

↓

Viral markers ***aren't detected***

e.g ***Herpes V*** in trigeminal ganglia

✓ Virus may be intermittently reactivated

↓

Can be ***recovered***

7-Virus shedding in the environment

Definition

The time at which the infected person

become **infectious to contacts**

Site

From body surfaces

involved in **viral entry**

No shedding

Occurs if ***the human is dead – end host***

↓

Not infectious e.g rabies

Atypical virus like particles

	Structure	Characters
Defective virus	Viral NA + capsid protein	***Can't replicate without a helper virus*** ↓ Provides the missing function
Pseudovirus	**Host** cell **DNA** + capsid	
Viroid	Circular RNA **without capsid or envelope**	
Prions	**Infectious proteins with no nucleic acid**	*Smallest infectious particle*

Laboratory diagnosis of viral infections

I-Direct demonstration of virus or its constituents in clinical specimens

1-Detection of viral particle by EM

For viruses of **special morphology** e.g *Rota virus*

2-Detection of specific Ag (Addition of specific Abs)

- ELISA
- RIA
- DIF

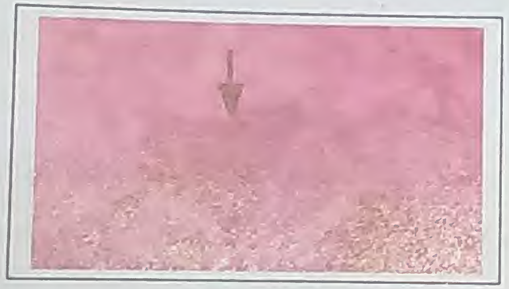
3-Detection of inclusion bodies (IB) by LM

Structure

Eosinophilic or **basophilic** bodies (Stained with **H&E**)

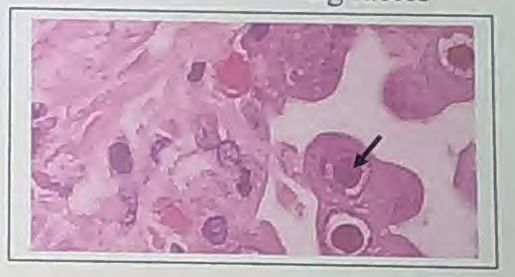
Etiology

- **Aggregation** of mature viruses
- **Degeneration** of host cells
- **Altered staining** at sites of viral synthesis



Site

- ***Intra-cytoplasmic*** e.g rabies
- ***Intra-nuclear*** Herpes
- ***Both*** Measles



4-Detection of viral genome by molecular techniques

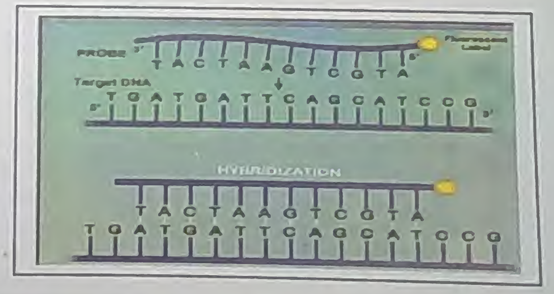
Polymerase chain reaction (PCR)

Idea

Amplification of specific NA sequence

Advantages

- ***Sensitive*** Detects minimal amount
- ***Specific***



Hybridization

Idea

Add **labeled NA probes**

Advantages

Specific

II- Serological detection of specific Abs

A- Types

IgM

Time

Appears ***early***

in infection

Significance

Recent

infection

Acute infection

IgG

Time

Appears **later**,

persists **longer**

Significance

Rising titer 4 folds

in paired serum samples

(10-14 days interval)

Acute infection

B-Methods

- ♣ Indirect ELISA
- ♣ Indirect immunofluorescense
- ♣ Radioimmunoassay (RIA)
- ♥ Complement fixation test (CFT)
- ♥ Neutralization test (Nt)

III-Virus isolation on living cells

A-Tissue culture

Inoculation of virus on

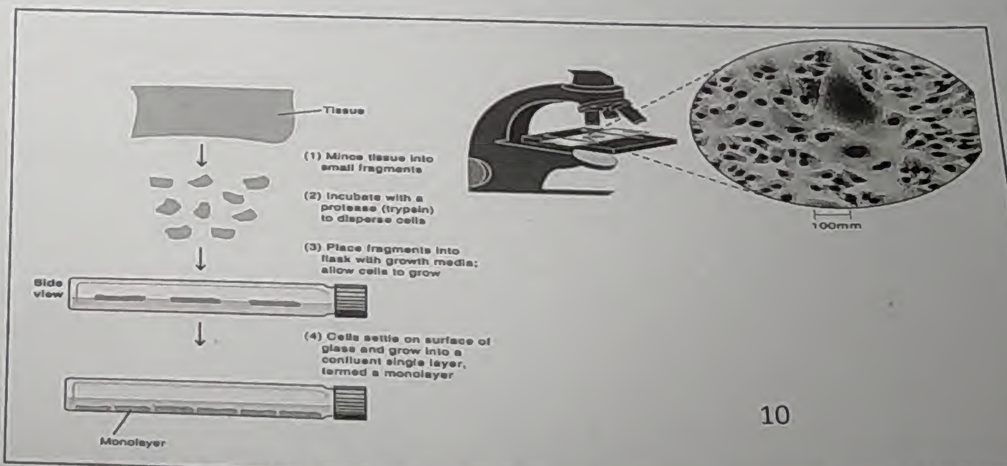
living susceptible cell culture

⬇

Virus infects the cell & replicates

⬇

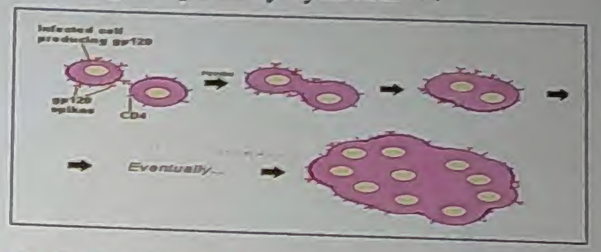
Viral growth is recognized by:



1 - Cytopathic effect

- ***Killing of cells*** → **Detachment** from wall of TC flasks
- ***Rounding of cells*** → e.g Herpes V
- ***Grape - like cells*** → e.g Adeno V

- ***Fusion of cells*** ***Syncitia (MGCs)*** → e.g Respiratory syncitial V.



2-Inclusion body formation:by L/M

- VICs stained with **H&E**
- e.g ***Negri bodies*** in rabies V.

3-Detection of viral Ags

On **surface** of **VICs**

By DIF

4- Detection of viral Nucleic acid

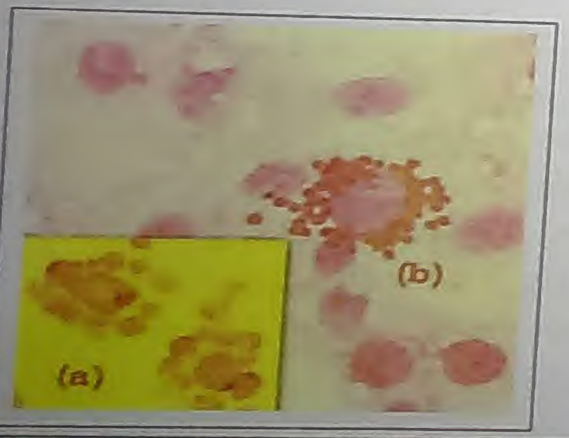
- ♦ ***PCR***
- ♦ ***Hybridization***
- ♫ Rapid
- ♫ Specific & sensitive

5-Heamadsorption

Adsorption of RBCs on VICs

Due to presence of viral **hemagglutinin**

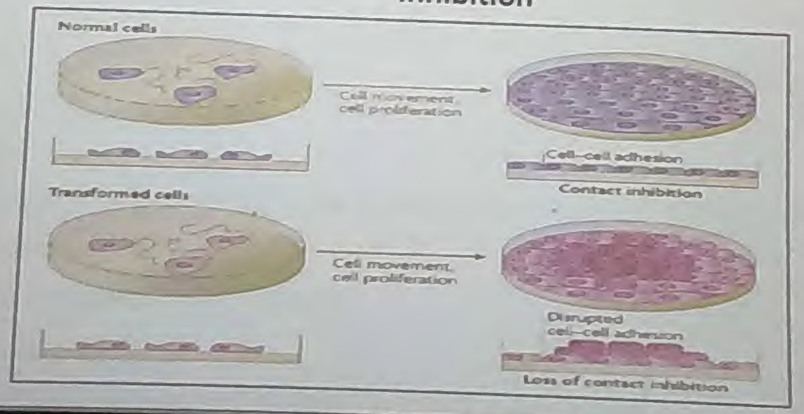
e.g Influenza&Parainfluenza V



6-Transformation

By oncogenic viruses

- **Uncontrolled** Growth
- Loss of **contact inhibition**
- **Piling up** of cells



7-Interference

Non cytopathic V.(e.g Rubella)

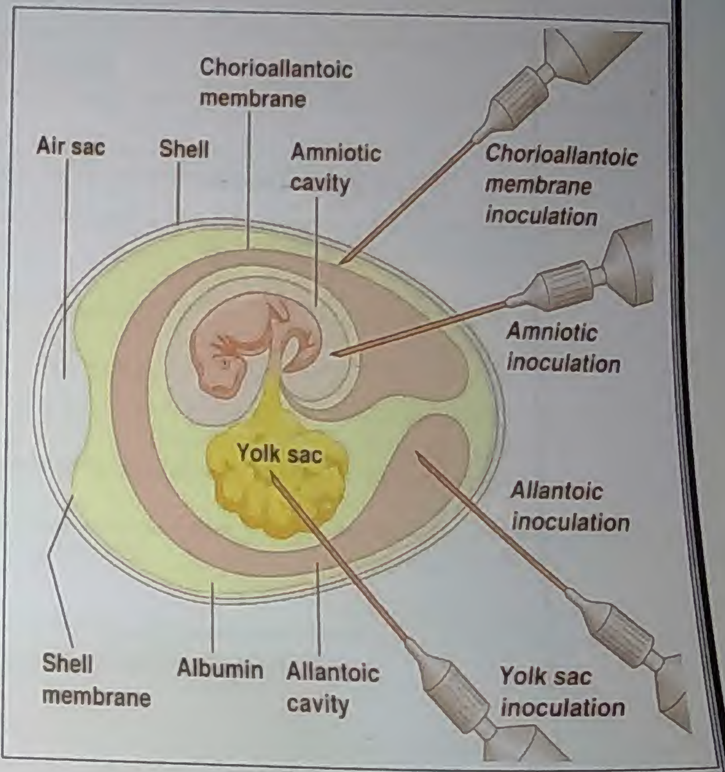
Interfere with replication & CPE produced by **cytopathic V.**

e.g Echoviruses

(added to TC as indicator)

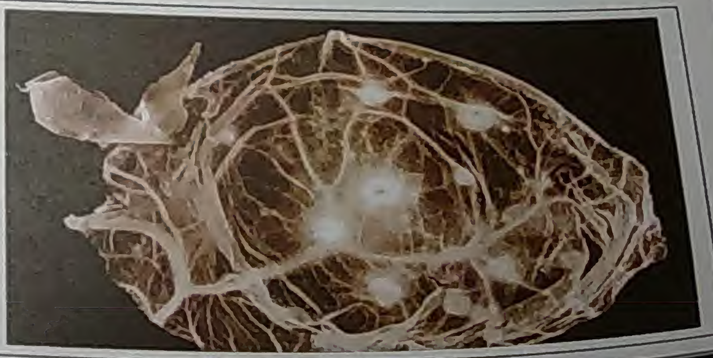
B - Laboratory animals & Chick embryo

	Laboratory animals	Chick embryo (rarely used)
1-Idea	Virus is inoculated **in laboratory animals** (e.g mice,rabbits or monkeys)	Virus is inoculated on **Yolk sac , amniotic sac or chorioallantoic membrane**
2-Identi-fication	*Ds or death of animal*	*i.Death of embryo* *ii.Production of hemagglutinin* *iii.Formation of pocks*
3-Uses		Mainly for viral multiplication ⬇ **Production of vaccines**



Essay Questions

1. Give an account on viral capsid.
2. Give an account on viral envelope
3. Give an account on eclipse phase of viral replication.
4. Give an account on inclusion bodies.
5. Give reasons : viruses exhibit tropism to different body tissue and cells
6. Compare and contrast between a systemic and a localized viral ds.
7. Compare & contrast between +ve & -ve sense RNA viruses regarding transcription & translation.



Reaction of viruses to physical & chemical agents

Agents	Effect on viruses		
A-Physical agents			
1-Heat	Destroy all viruses at **60C for 30 min except hepatitis A&B viruses**		
2-Coldness	i.Most viruses are stored at: **- 40 or -70 (better)**	*Lyophilization* Dryness+freezing under vaccum ⬇ Preserve viruses at 4C for years	**Some V** are inactivated by ***freezing***
3-Radiation	***UV rays , X rays & γ rays*** (high energy particles) **affect NA** of viruses → inactivation		
B-Chemical agent			
1-pH	✓ Viruses are stable between 5&9	✓ Enteroviruses are resistant to acidity	☒ All viruses are *destroyed* ***by alkalinity***
2-Ether, alcohol & other detergents	Dissolve viral envelope → *inactivate* ***enveloped viruses***		
3-Oxidizing agents	**e.g Chlorine ,iodine & H_2O_2** → *Inactivate viruses*		
4-Formaldehyde	Affect NA without affecting viral Ags → Used to *prepare* ***inactivated vaccine***		
5- Salts e.g $MgCl_2$	***Stabilize viruses in live attenuated vaccines*** e.g Poliomyelitis vaccine ⬇ Maintain potency for ws at high temperature in tropics		
6- Glycerol (50%)	*Preserve viruses* , ***but destroy bacteria*** → used to **decontamiante** viral preparations		
7- Antibiotics	*No effect on viruses* , but **kill bacteria**		
8-Phenols	Most viruses are *resistant*		

Virology 2

DNA VIRUSES

DNA Viruses

Enveloped		Non enveloped
Herpes family	Pox family	
1-Herpes simplex type 1&2 (HSV1&2) **2-Varicella-Zoster virus** (VZV) ***3-Human herpes type 6,7&8*** (HHV 6,7&8) 4-Epstein-Barr (EBV) & Cytomegalo (CMV)	**1-Small pox & Vaccinia** ***2-Molluscum contagiosum***	***1-Human papilloma (HPV)*** 2-Parvovirus B19 3-Adenoviruses 4-Polyoma viruses

Skin & MM infections

Herpes Simplex viruses		Varicella-Zoster virus		HHV 6&7	Pox viruses		Non enveloped V
HSV1	HSV2	Varicella	Zoster		Small pox	Molluscum	Human papilloma
♦*Oropharyngeal* ♦*Skin* :fingers	*Genital* (Oncogenic)	*Generalized* rash	*Localized* rash	*Localized* rash	*Generalized* rash	*Skin wart&Genital* lesions Benign	Oncogenic
	Neonatal	Neonat. & cong.					Neonatal
❖ **CNS:** encephal. ➢ Pneumonia	**CNS**:menig.	**CNS**:encephal. Pneumonia	**CNS**: CN				

General characters of Herpes family

A - Pathogenesis & disease

Infections

Most are **asymptomatic** ↔ Severe in **IS**

Latency

Remain **latent** in host after 1ry infection

Sensory ganglia ↔ ***WBCs***

•HSV1,2,VZV ♦ EBVCMV, HHV6,7&8

Oncogenic

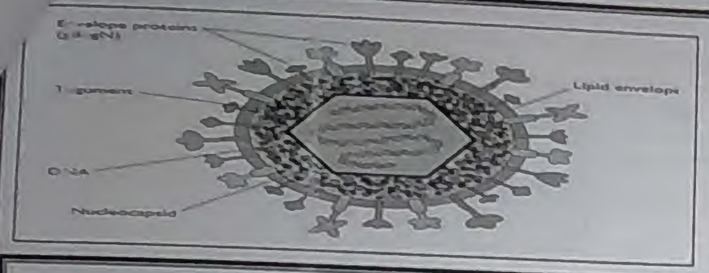
HSV-2	HHV8	EBV
Cancer cervix	*Kaposi sarcoma*	♠ *Burkitt's lymphoma* ♠ *Nasopharyngeal carcinoma*

B - Effect on Tissue culture

Cytopathic effect (CPE) → **Death** of cells

Rounding — Ballooning — Fusion → ***Multinucleated giant cells***

Intranuclear IB



Herpes simplex viruses type 1 & 2

Common features between HSV1 & 2

	HSV 1		HSV2
1-Same structure	**i-Genome :** Ds DNA	**ii.Capsid :** Icosahedral	**iii.Enveloped**
2-Reactivations are common by :	***i.Physical*** ♦ Sunlight (long exposure)	***ii.Physiological*** ♠Stress ♠ Menstruation ♠Pregnancy	***iii.Pathological*** ♣↓ immunity ♣ High fever ♣ Common cold
3-Pathogenesis : *1ry infection& Latency*	Virus replicates in the **skin or MM** at the site of infection ⬇ Migrates ***up the neuron*** → *latency in* ***sensory ganglia***		
4-Immunity	Abs don't prevent reactivation as viruses are **hidden in neurons**		

Differences between HSV1 & 2

	HSV1	HSV2
1-Genome	**RE** analysis of DNA	
2-Type specific Ag	Detected by specific **monoclonal Ab**	
3-Lesions	***Above*** the waist	**Below** the waist
4-Modes of transmission	***Contact*** with infected vesicle or saliva	☺ **Sexual** ☺ From **infected maternal genitalia** to newborn
5-Latency	***Trigeminal ganglia***	**Lumbar or sacral ganglia**

Diseases caused by HSV1

A - Recurring lesions

1-Oropharyngeal lesions

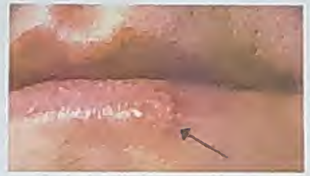
i.Acute gingivostomatitis

- ***1ry*** infection in ***childhood***
- By kissing from older person
- ***Generalized :*** painful vesicles in oral cavity
- Ulcer → Sponataneous healing in 2 ws

ii.Herpes labialis

(fever or cold sores)

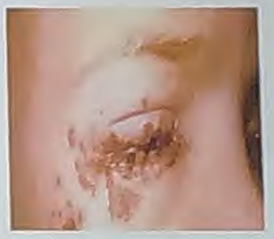
- ***Recurrent*** form
- ***Milder*** Localised vesicle in lips or nose



2-Herpetic keratoconjunctivitis

i.1ry infection

Ulcers in cornea & eye lids



ii.Recurrence

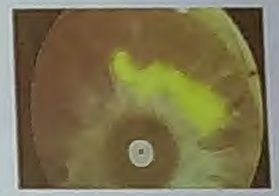
Dendritic ulcer

↓

Corneal scarring & opacity

↓

Blindness



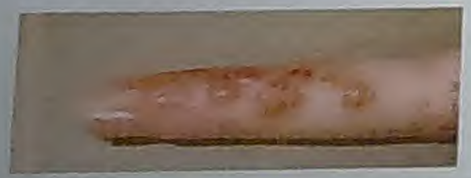
B - Other lesions

1-Skin ds

i.Herpetic whitlow

Fingers contact with infected vesicles

- ✓ Dentists
- ✓ Nurses
- ✓ Thumb-sucking children



ii.Eczema herpeticum

Vesicles on **eczematous** children

2-CNS infections

Encephalitis

in **temporal** lobe

↓

Fatal

3-Disseminated infection

Pneumonia

in IS pts

Diseases caused by HSV-2

1-Genital lesions

- **Sexual**
- **Vesicles&ulcers in**
  - ♦ Penis
  - ♦ ***Cervix***
  - ♦ Vagina
- **Dysuria & Inguinal LN ++**

2-Neonatal herpes (75% by HSV2)

- ♠ ***In uterus***
- ♠ ***During*** *birth*
- ♠ ***After*** birth

(contact with infected family member or HCWs)

- **Disseminated ds**
  - • Eye
  - •Mouth

± skin lesions

- • ***Encephalitis***

3-Aseptic meningitis

Self limited

Varicella Zoster virus (VZV)

Varicella (Chiken pox)		Zoster (Shingles)	
1ry inf. in childhood	*Generalized*	*Reactivation*	*Localized*

Congenital & Neonatal Varicella

	Congenital Varicella	Neonatal Varicella
1-Acquisition	During **1ry** maternal infection, virus **crosses placenta** in **1st** trimester	i.**Last week** of pregnancy. ii.Just **after birth**
2-Lesions	**Fetal** malformations	**Disseminated** Varicella

Comparison between Chicken pox & Small pox

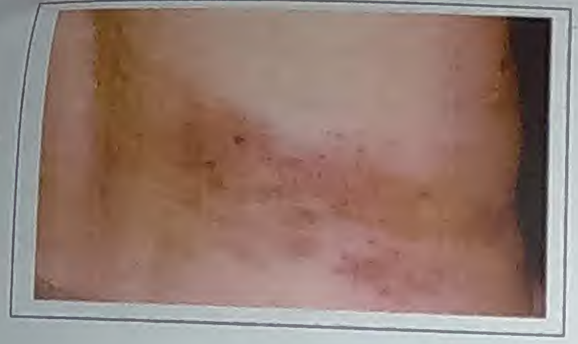
	Chicken pox :Herpes family	Small pox :Pox family
1-Pathogenesis	i.Virus infects mucosa in upper RT → Local LNs ↓ 1ry transient viremia → inf.of RES : liver & spleen ↓ *2ry* viremia → ***generalized rash***	
	ii.Latency In ***dorsal root*** or ***trigeminal*** ganglia (nerve) ↓ Reactivation → **Zoster**	**ii.No latency**
2-Mode of transm.		
a.Droplet	From case of Varicella	From case of small pox
b.Contact with vesicles	From case of Varicella or Zoster	
3-Clinical picture	Mild fever	
Rash	**Stages** : macule → papule → vesicle → pustule → crust	
i.Distribution	**Centrifugal** 1st on trunk ↓ face & limbs 	**Centripetal** : 1st on face, arms & legs ↓ hands & feet 
ii.Stages	**Cropping :** all stages are detected simultaneously 	**No** cropping 
iii.Fate	Crust → healing → **no scar** ✓ The ds is more ***severe*** in ***adults***	Crust falls → **permanent scar** (Pt is contagious until crusts fall off)

Complications of Chicken pox(most pts recover rapidly)

i.Pneumonia &keratitis in IS or adults pts

ii.Reye's syndrome (rare)

Encephalitis & hepatic ds following ***salicylate*** intake



Zoster (Shingles)

A-Etiology (sporadic)

Reactivation of latent VZV in

Adults ⟷ IS pts

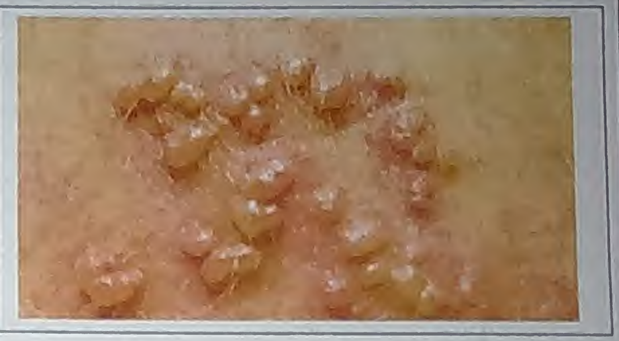
B-Clinical picture

Severe pain

↓ Few days

Rash similar to Varicella but

Unilateral ⟷ Limited to skin *innervated by* ***dorsal root ganglion***



C-Complications

Eye via trigeminal nerve: HZ ophthalmicus			**Post herpetic neuralgia**		**Rare complications**	
Conjunctivitis	Keratitis	**Iritis**	**Severe debilitating pain** in affected areas even after clearance of rash	Duration •Few ws or ms usually •Many yrs rarely	⋆Blindness ⋆Hearing loss	⋆Pneumonia ⋆Encephalitis ⋆**Death**

Causes of eradication of small pox (since 1980)

Control of transmission

- **Diseased** individuals are the **only source**
- **No animal** reservoir or **carrier**
- **Easy** diagnosis

Efficient IR

- **Single stable** serotype → Long lasting immunity
- **Efficient** live **vaccine**

Small pox is notable in medicine history

- *1st* **vaccine :** ***Live attenuated vaccinia virus*** Given to children by scarification
- 1st eradicated ds
- Potential use as **biological weapon**

Treatment

	HSV 1& 2	VZV
1-M. of action	*Acyclovir* ⊖ viral **DNA polymerase** ⟶ Doesn't affect virus in latent stage	
2-Selectivity	Affect only **VIC as viral thymidine kinase** activates the drug	
3-Indications	**i.Eye & skin** lesions : topical **ii.Reactivation** of **latency** in **IS** pts : IV	***i.IS*** children ***ii.Zoster*** pts ***ii.Complicated*** Varicella : Pneumonia & keratitis ***iii.Neonatal*** Varicella

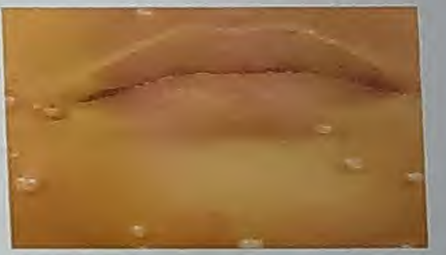
Prevention

	HSV 1& 2	Varicella (Chicken pox)	Zoster
1-General	1 - Avoid **contacts with skin** lesions		
	2-Ceserian section : For pregnant ♀ with genital herpes Prevent neonatal herpes		
2-Chemoprophyl.	**Acyclovir** : For ***IS pts*** e.g transplant recipients Prevent reactivation		
3-Vaccine			
a. Type		***Live attenuated SC*** (Zoster Vac.contains 14 times more virus than Varicella Vac.)	
b.Administration		2doses for children between 1-12 yrs	1dose > 60 yrs
c.Contraindications		i.Immunocompromised people ii.Pregnant ♀	
4-Passive		***Specific VZ Igs*** **1.IS children**:exposed to inf. **2.Infected pregnant ♀**: i.Before delivery ii.Their newborns; immediately after delivery	

Laboratory diagnosis

I-Specimen	HSV	VZV	Small pox
	1 - Vesicular fluid		
II-Direct virus demonst.	2-Scrapping from ulcer or cornea		
A-EM	Detects viral **particles**		
B-LM (Rapid & diagnostic) 	***i.Multinucleated giant cells*** : Using **Tzank smear** Cells from vesicles stained with Giemsa  ***ii.Intranuclear IB : Cowdry bodies***		Detects viral particle
C-DIF	Detects viral **Ag**		
D-PCR	Detects ***DNA in CSF***	Detects DNA in vesicles	
III-Virus isolation	*On tissue culture :* **CPE** & **Intranuclear** IB		*On chick embryo (most reliable)* in chorioallantoic membrane: **Intracytoplasmic** IB + **pocks** 
IV-Serology : ELISA	1-Ig **M**: ***1ry*** (current) infection 2-**IgG**: ***past*** infection (Recurrence isn't associated with ↑ IgG)		**Specific Ab** Confirm diagnosis

Human papilloma virus | Molluscum contagiosum V.

1-Structure		
a.Genome &Capsid	DsDNA& Icosahedral	
b.Envelope	Non enveloped	**Enveloped**
c.Types	**> 60** types according to **DNA homology**	
2-Modes of trans.	**i.Cutaneous** lesions : *direct* contact or through *fomites* **ii.Genital** lesions : sexual transmission	
3-Pathogenesis	Epithelial proliferation	
	i.Cutaneous → self limited ***ii.Genital → oncogenic***	Non oncogenic
4-Disease	**a.Cutaneous infections** : common warts ♠ Hands ♠ Soles (plantar warts) 	Benign **wart-like** lesions on face,arms&genitalia **Spontaneous healing** in 2-6 ws ***No malignancy*** 
	b.Mucosal infections ***i.Condyloma accuminata (type 6&11)*** Malignant in IS pts → Invasive squamous epithelioma  ***ii.Juvenile laryngeal papilloma*** From mother birth canal infected with genital warts  ***iii.Cancer cervix : type 16 & 18***	✓ NB.virus is **weak** Ag → **No serological** tests
5- Laboratory diagnosis	Direct demonstration of virus in specimen **i- PCR** : detects viral DNA	
	ii-Hybridization	***ii.EM*** : detects viral particle
6-Treatment	**NO** antiviral drugs	

Vaccine for HPV

Type

Recombinant quadrivalent

Types 6,11,16 &18

Indications

Girls &women

(11-26)

Effects

Prevents:

i.Cervical cancer

ii.Anogenital warts

Human Herpes Viruses 6 & 7

Characters & Disease

Age affected

All children by age of **two**

Saliva of majority of adults

Life long

Disease

Roseola infantum (6th ds)

(Exanthem subitum)

Maculopapular rash on ***trunk &neck***

Latency

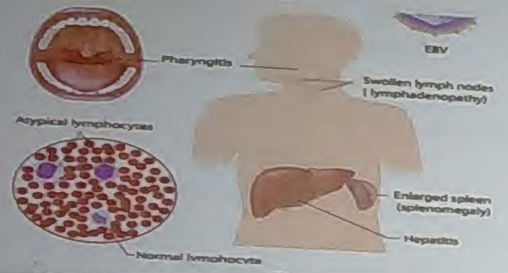
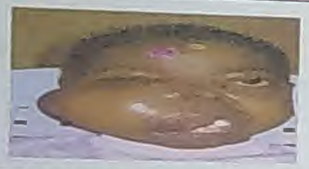
T cells

(T-lymphotropic)

RES & BLOOD infections

Epstein Barr Virus (EBV)	**Cytomegalovirus (CMV)**	**Parvovirus B19**
Infectious mononucleosis		***Anemia***
	Congenital infections	
Oncogenic		**Skin rash** :localized

	Epstein Barr Virus	Cytomegalovirus
I - Structure	i. Ds DNA ii.Icosahedral capsid iii.Envrloped	
II - Pathogenesis		
A-Acute infection	Virus infects nasopharyngeal epithelium ↓ Spread to **salivary glands** & oropharyngeal L.T ↓ ***Infects B lymphocytes that spread the virus*** ↓ Viremia ↓ Infection of more lymphocytes & RES (liver&spleen)	Virus infects upper RT& **local lymphocytes** ↓ ***Lymphocytes spread the virus*** to other lymphocytes & monocytes in spleen and LNs ↓ Viremia ↓ Spread to a variety of epithelial cells **i.Salivary G .ii.Kidney tubules iii.Testes & ovary**
B-Latent infection	**⋆B cells & Oropharyngeal epithelium** ❖ ***Tumor formation*** Integrates in host chromosome (sometimes) ↓ Indefinite cellular proliferation	**Monocytes & lymphocytes**
C- IR	1-Elicits both **CMI (main)** &**HI** → maintain virus in a **latent** state → **Reactivation** in **IS**	
	***2-Atypical T lymphocytes*** **CTLs** destroying virally infected B cells → ↓ their n	
III - Modes of Transmission	**Intimate contact with infected saliva (main)** *Kissing ds* NO KISSING! 	**1-Close contact with body secretions as saliva,** urine, vaginal secretions & semen **2-Blood** transfusion **& transplacental** 3-Organ **transplantation** (liver & Kidney) **4-Sexual** intercourse **5-Perinatally** : i.Passage in infected birth canal ii.Breast feeding

III-Diseases	EBV	CMV
A-Normal host		***1-Asymptomatic in older children & adults*** Affects **95%** of normal population **Flu**-like symptoms ***2-Infectious mononucleosis syndrome (self limited)*** i.Fever & **pharyngitis** ii.**L**ymphadenopathy iii.Hepatosplenomegaly , **hepatitis** ± jaundice **iv. +ve heterophil Abs** :Abs agglutinate **Sheep RBCs** / iv. -ve heterophil Abs
B-Immuno-compromised host	♦ Transplanted pts ♦ AIDS pts ♦ Pts receiving IS drugs ***More severe*** ds 	***1-Pneumonia*** 2-Rejection of renal & liver allografts **3-Retinitis → blindness** 4-Encephalitis,colitis &oesophagitis
C-Other diseases	*Malignancies:* 1-Burkitt's **lymphoma** **2-Nasopharyngeal** carcinoma	***Congenital &neonatal infections***

A - Congenital infections of CMV

1-Modes of transmission : in uterus

With both **1ry & reactivated** maternal inf. ⟷ At **any stage** of pregnancy

2-Effects

Abortion or Stillbirth

Cytomegalic inclusion disease (CID)

CNS

•*Brain calcification* •*Microcephaly* •*Mental retardation*

Retinitis & Ocular defects

Deafness

Hepatomegaly & Jaundice

B - Perinatal infections

1-Modes of transmission : a.From birth canal b.Breast milk

2-Effects

Asymptomatic (usually)

Infected neonates have **high titers** of **maternal Abs(IgG)**

Hepatitis & pneumonia (uncommon)

Parvovirus B 19

Structure

- Small
- SS RNA +ve sense or –ve sense
- Icosahedral
- Non enveloped

Modes of transmission

- Droplet
- Blood **transfusion** & blood **products**
- **Transplacental**

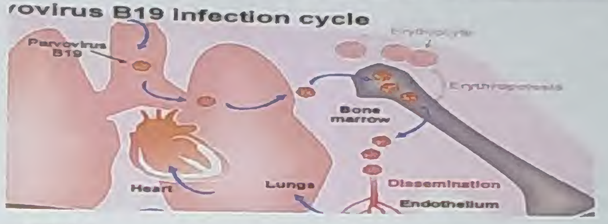
Pathogenesis

Target & Replication

Immature RBCs in adult BM&fetal liver

↓

Interruption of RBCs production



Immunity & Persistence

Ab neutralize the virus

↓

Persistence of infection

in ***immunocompromized*** pts

Disease production

1-Erythema infectiosum (5th ds) : most common

IC deposition

- ***Slapped cheek rash*** in children
- ***Arthritis*** in adults

2-Anemias

Transient aplastic crisis (TAC)

- ***Temporary*** arrest of RBCs production
- Apparent only in pts with ***chronic hemolytic*** *anemia*

TAC

Pure red cell aplasia (PRCA)

- **Persistent** inf. ***Severe chronic*** anemia
- In **IC** pts

PRCA

Non immune Hydrops (erythroblastosis) fetalis

Congenital inf.

from ***10th*** to ***20th w*** of pregnancy

↓

Arrest of fetal **RBCs** production

↓

Severe anemia

Laboratory diagnosis

	EBV	CMV	Parvovirus B19
I-Specimen	1-Peripheral **blood mononuclear** cells 2-**Saliva**		1-**Blood cells** 2-**Respiratory** secretions
	3-Lymphoid tissue	***3-Urine***	***3-Tissue samples***
II-Direct detection			
A-PCR	Detection of viral DNA → **most sensitive** method → **routine detection**		
B-Detection of Ag	**DIF & ELISA**		
C-LM		1-Multinucleated ***giant*** cells 2-***Intranuclear owl's eye*** IB 	
III-Serology			
A-Specific Abs:ELISA	**Anti VCA** (viral capsid Ag)		
1-IgM	***Recent infection***		
2-IgG	Persists for life → indicates ***past** infection **&potential for reactivation***		
  	**B-Non specific heterophil Abs** By ***Paul Bunnel & monospot tests*** **Transient** Abs in acute infection Agglutinate **sheep RBCs**		
	IV-Blood picture		
	1-Absolute ***lymphocytosis*** ***2-Atypical T lymphocytes***		

Treatment

CMV	Parvovirus B19
In IS pts **Gancyclovir** 	In IS pts (PRCA) **1-Blood transfusion** **2-Ig preparation** Neutralize viruses ↔ Cure persistent inf.

Prevention

CMV	Parvovirus B19
1-Screening	
of transplant donors &recipients for ***CMV Abs***	of blood donors
2-Good hygienic practices e.g careful hand washing	
After contact with diapers or oral secretions	**Prevent spread** through respiratory secretions & fomites
3-Isolation of newborn with CID from other newborns	***3-Standard inf.control precautions*** **Protection** of HCWs from pts with **TAC** or chronic **PRCA**

No antiviral treatment or **specific** prevention for **EBV**

Other infections

Adenoviruses	HHV 8	Polyoma viruses

Adenovirus

Structure

Genome: Ds DNA

Capsid : Icosahedral & carries fibers with knobs

Non enveloped

Attachment of virus — Type specific Ag: 52 serotypes — Heamagglutination

Mode of transm.	Pathogenesis	Prevention
	A-Replicate in epithelium of:	
1-Droplet	*1-RT*	i-Avoid **overcrowding** ii.Live attenuated **oral vaccine** for military (ceased in 1996)
2-Contam. eye equipements & Direct contact	2-Eye	iii.Adequate **sterilization** of solutions& equipements used in **eye examiantion** iv.**Chlorination** of swimming pools
3-Fecooral	*3-GIT&UT*	v.Proper **hand hygiene**
	B-Virus may invade blood In early stage of ds	
	C-Most inf.are asymptomatic Virus may remain latent for life in adenoids	

Laboratory diagnosis

A-Specimen

Swabs : Throat , conjunctiva , rectum

Stools or urine

B-Identification

Direct virus demonstration

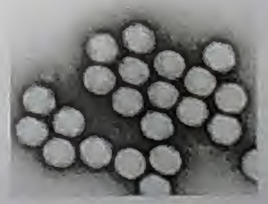
- EM: Viral particle
- PCR: Viral DNA

Virus isolation

On human epithelial cells (slow)

CPE : *grape like* rounded cells

Serotyping by *HIT*



Serology : CFT

Rising titer of IgG (4folds) in 2 samples

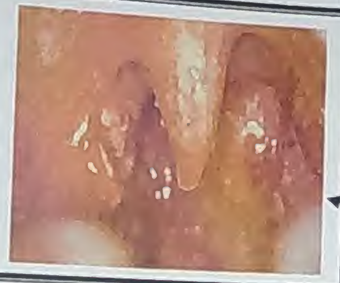
Diseases (acute & self limited)

I-Respiratory & Eye diseases

Respiratory ds

1-Febrile respiratory ds (common cold)

Children: usual manifestation



Running nose,dry cough & **pharyngitis**

2-Acute respiratory ds (ARD)

Military groups

Cough,pharyngitis → ***Pneumonia***

3-Pneumonia : in hospitalized children (nosocomial)

Eye ds

1-Acute pharyngoconjunctival fever (APC)

Children: *Outbreaks* due to *insufficient chlorination* of swimming pools

Pharyngitis & ***conjunctivitis***

2-Epidemic keratoconjunctivitis (EKC)

Adults: By contaminated *eye instruments* (highly infectious)

Conjunctivitis → ***keratitis*** → ***corneal opacity***

3-Conjunctivitis

II-GIT & UT ds

GIT

Infantile gstroenteritis

By types **40 & 41**

UTI : Hgic cystitis (reactivation of dormant virus or nosocomial spread)

Children (commnest cause)

Aged 5-15yrs & boys > girls

IS adults

Kidney or BM <u>transplantation</u> ↔ <u>AIDS</u>

III-Severe infection in IS pts

Transplant pts

Pneumonia (fatal) ↔ ***Hepatitis*** in liver allograft

AIDS

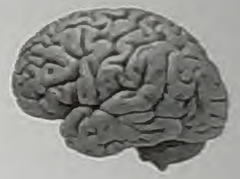
Gastroenteritis

Polyoma viruses

Structure

- Ds DNA
- Capsid :**icosahedral**
- **Non** enveloped

Members & Diseases

BK virus	**JC virus**
1-1ry subclinical inf. in childhood → **Persist (latent)** in healthy individuals	
in ***kidneys***	in ***brain***
	
2-Reactivation in IS pts	
Nephropathy & ***rejection*** of renal grafts	Progressive ***multifocal leukoencephalopathy*** → fatal

HHV8 (Kaposi sarcoma associated herpes virus)

❖ **Oncogenic with AIDS**

- ***Kaposi sarcoma***
  Endothelial cell tumor
- Body-cavity based ***lymphoma***

❖ **Diagnosis**

PCR

Viral DNA

Essay Questions

1-Give an account on human papilloma virus as regards structure, ds produced and laboratory diagnosis.

2-Prophylaxis of human papilloma virus

3-Mention causative org. ,mode of transmission and clinical picture of : Condyloma accuminata ,dendritic ulcer of cornea and non immune hydrops fetalis

4-Discuss viral structure and laboratory diagnosis of cytomegalovirus.

5-Mode of transmission and pathogenesis of Varicella zoster virus

6-Describe laboratory diagnosis of herpes simplex virus.

7-Compare & contrast VZV &CMV as regards site of latency & mode of transmission

8-Mention specific laboratory tests used in diagnosis of infectious mononucleosis and their significance

9-Give an account on general characteristics of herpes viridae family

10-Laboratory diagnosis of infectious mononucleosis.

11-Describe pathogenesis of HSV 1& 2.

12- Give reason:

a. antiviral drugs don't eliminate latent stage in herpes infection.
b. Parvovirus B19 is a serious infection in pts with chronic hemolytic anemia

13-Mention the causative org. and mode of transmission of :

a.Shingles

b.Infectious mononucleosis

14-Mention the value of the following laboratory tests:

a. Monospot test in diagnosis of infectious mononucleosis.
b. Tzank smear in diagnosis of Herpes simplex.

18'

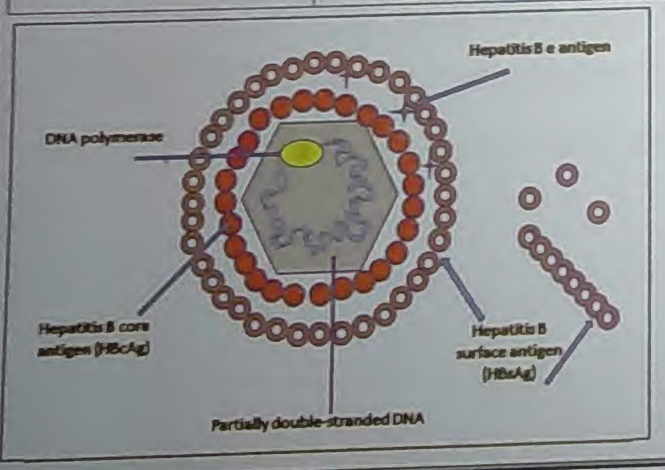
Virology 3

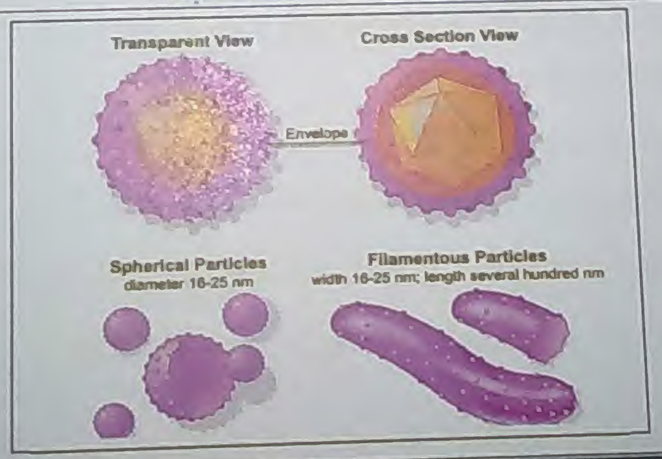
Hepatitis Viruses

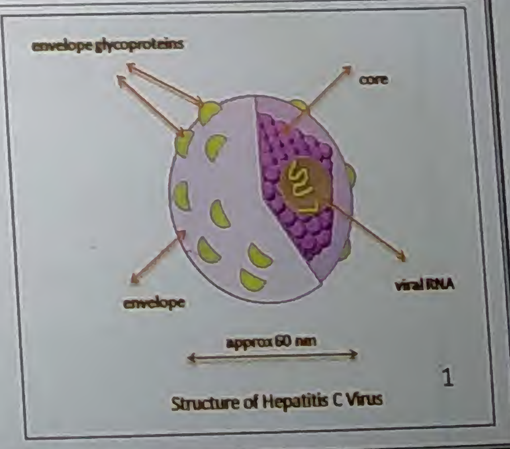
Hepatitis viruses :Viruses that infect the **liver as 1ry target organ**

- **Genome**
  - **RNA** : A , C, D & E
  - **DNA** : B
- **Transmission**
  - **Parentrally** : B,C & D
  - **Enterically** : A&E

	HBV	HCV
Structure		
A-Family	**Hepadna** viruses	**Flavi**virus
B-Core	**1-Partially DS** DNA **2-DNA polymerase** **3-Core Ags** : c Ag & e Ag	**1 - SS**RNA **+ ve** sense **2 - 6 genotypes** : *type 4* is predominant in Egypt
C-Capsid	**Icosahedral**	
D-Envelope : Host derived lipid bilayers	**1. S Ag** i . Attachment of virus → Vaccine preparation ii . Presence of virus → Diagnosis **2 . 3 forms of HBV** are detected in pt serum **Complete** virion = **Dane** particle **Secreted S Ag** without DNA: • Spherical • Filamentous	Carries viral Ag







Structure of Hepatitis C Virus

	HBV	HCV
Modes of transmission	**1 - Parentrally** (injured skin &MM) : blood & Blood products,sharing razors or toothbrushes **2 - Perinatally** : in uterus & during birth **3 - Sexual intercourse** **4-Organ transplantation**	
Pathogenesis		
A-Entry &spread	1-Enter & spread by **blood** to liver → Multiplication in hepatocytes **2-No CPE** : infected cells are damaged by ***CTLs***	
B-Fate	**15%** of pts become **chronic** carriers (***S*** Ag in blood **≥ *6*** ms)	**85%** of pts become **chronic** carriers
Chronic carriers	1 - Asymptomatic mostly **2 - Chronic active hepatitis** → cirrhosis → ***liver failure*** and /or ***HCC***	
Immunity	**Anti S** → life long immunity	
Cl.picture	**Serum** Hepatitis	**Non A non B** hepatitis
A - IP	1.5 m-6 ms (Symptoms are ***more severe***)	2 ws-6m (***80%*** of inf.are ***asymptomatic***)
B - S & S	1- Fever, anorexia & vomiting **2- Jaundice** ,dark urine & pale stools	
Treatment (chronic cases)	**1 - α interferon** ***2 - Lamivudine*** : nucleoside analogue	1- **α interferon + Ribavirin + Sofosbuvir** (sovaldi): ⊖ *viral RNA polymerase* **2-Harvoni :** ***Sofosbuvir + Ledipasvir*** (⊖ *NS5A protein important in replication)* •**Duration** *:12-24 ws (depends on viral count,genotype & cirrhosis)* •**Monitoring**: ***Quantitative PCR*** *(4ws,end of ttt,12ws after completion)*

Laboratory diagnosis of hepatitis B

I - Non specific tests : Marked ↑ in liver transaminases & bilirubin

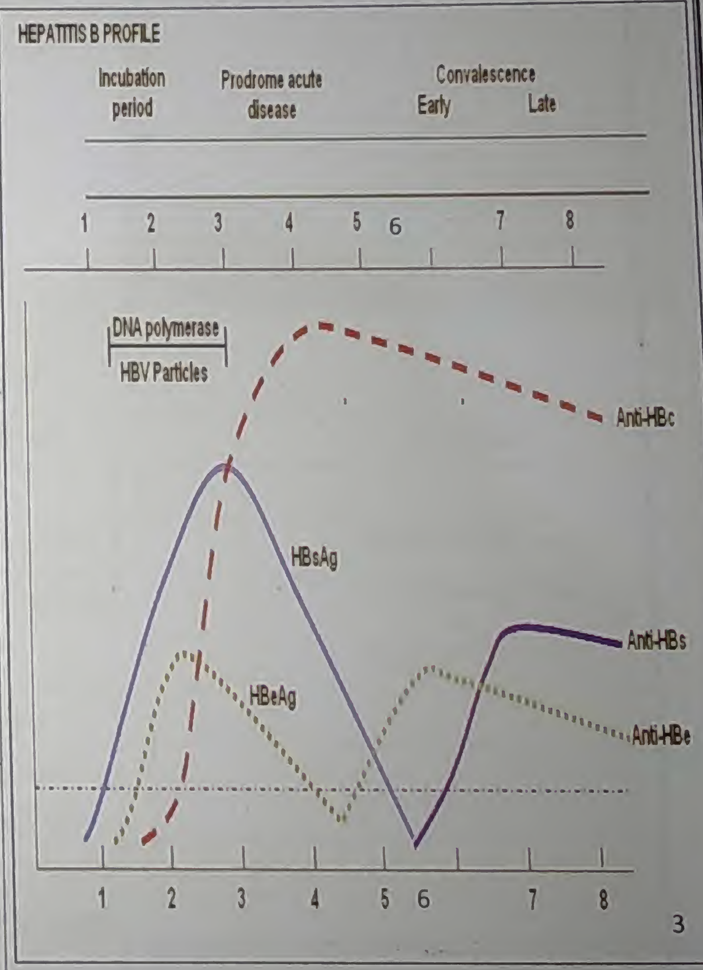
II - Specific tests

A-Hepatitis B panel : in serum

Detection of *HB Ags* (by direct ELISA) & *HB Abs* (by indirect ELISA) in serum

Marker	Time of detection	Significance	
1-sAg	1st m (I P) → ↓in 3 ms ↓ Disappears **after 6 ms** except **in chronicity**	*i.Acute* inf.	*ii.Chronic* inf.
2-sAb	After disappearance of S Ag ↓ **For life**	*i.Resolution* of inf.	*ii.Immunity* against reinf.
3-cAb			
a..IgM	Clinical onset ↓ Disappear **after 6ms**	*i.Acute* inf. (with SAg)	*ii.Window phase* (without SAg)
b.IgG	After disappearance of IgM ↓ **For life**	*i.Chronic* inf. (with SAg)	*ii.Past* inf. (without SAg)
4-eAg	I P ↓ Througout **acute illness**	*High infectivity of pt (best marker)* ↓ Its disapp. is a good prognostic sign	
5-eAb	After disapp. of eAg	*i.Low risk* of transmission	*ii.Recovery*

Persistence of eAg & absence of eAb indicate *chronic active hepatitis* → need for ttt



NB : cAg

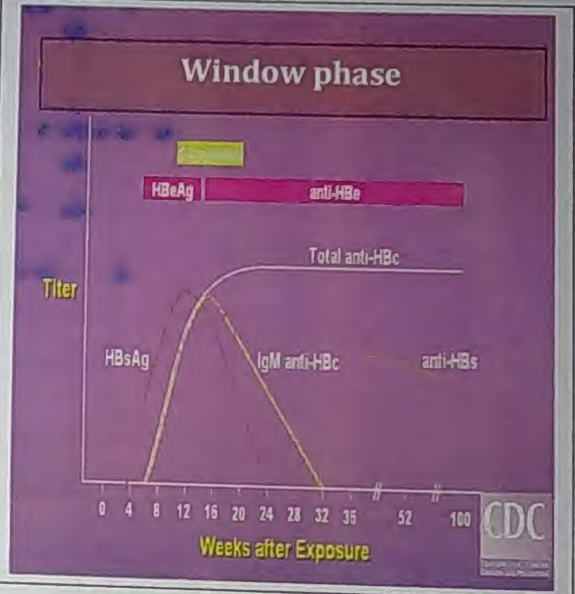
Detected only in **hepatocytes** (not in serum) **by immunohistochemistry**

Window phase (in some pts)

Etiology	Characters	Time	Diagnosis
Delayed rise of anti-S Abs	***No S Ag or S Abs*** are detected	6-8 ms after infection	***Anti c IgM***

B - PCR : Detects viral DNA in blood

- Indicates **viral replication**
  - Need for ttt
  - Follow up ttt
- +ve in chronic inf.



HBV Panel interpretation

Test				Interpretation	Notes
HBs Ag	**HBcIgM**	**HBcIgG**	**HBsAb**		
+ve	**+ve**	-ve	-ve	**Acute** HBV infection	***HBV DNA +ve + HBeAg +ve*** ↓ high infectivity
+ve	-ve	**+ve**	-ve	**Chronic** HBV infection	
-ve	**+ve**	-ve	-ve	**Window** phase	
-ve	-ve	**+ve**	**+ve**	**Immune** person due to **previous infection**	
-ve	-ve	**-ve**	**+ ve**	**Immune** person due to **vaccination**	
-ve	-ve	-ve	-ve	**Susceptible individual**	

Laboratory diagnosis of HCV

I - Non specific tests : Marked ↑ in liver transaminases & bilirubin

II - Specific tests

ELISA : Detection of Abs inserum

1' **Positive**

2 Doesn't differentiate between current (acute or chronic) inf. or resolved (cured or past)) inf. or false +ve (no infection)

Negative 1 – – ▸ 10 **No infection** except if the pt is in the window period (delay in seroconversion up to 6 ms)

3 ***RT-PCR*** : Detection of viral RNA in pt serum

Positive 4

Current HCV inf.

6 **Negative** – – ▸ **No current** infection

RIBA 7

Conf.for Abs

8 **Positive**

Cured (past) inf.

Negative 9

False +ve ELISA

5 **Advantages of PCR**

1-Demonstrate active viral repliaction in serologically confirmed cases ⬇ Need therapy

5' 2-Follow up response to ttt

10' 3-Diagnose early cases before seroconversion

Disadvantages of PCR 5"

Doesn't differentiate between acute (recent) & chronic inf.

■ Screening blood donors in blood banks :

Combined Ab testing & Ag detection or RT PCR is recommended to avoid missing blood donors in window period

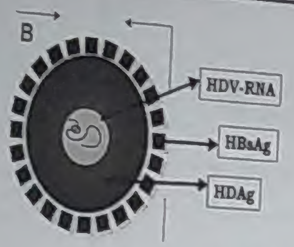
5

Hepatitis D Virus

Virus structure

SS RNA :

-ve sense



Delta Ag

Defective virus

Lack gene coding for envelope protein

Replication only *in cells infected with HBV(helper virus)*

Use **S Ag** as envelope protein

Pathogenesis & Cl.P

A-Mode of transmission , Entry & spread : as HBV (E).

B-Effect :↑ severity of HBV infection

Coinfection with HBV

↑ possibility of **fulminant hepatitis**

Superinfection on top of HBV

↑ rate of chronic active hepatitis & cirrhosis to 80%

Prevention

of coinfection

HBV vaccine

of superinfection

Avoid IV drug abuse

Laboratory diagnosis

RT PCR

Detects ***viral RNA***

ELISA

Detects ***Delta Ag*** ↔ Detects ***IgM*** or ***IgG to Delta Ag***

Reaction of HAV & HBV to physical & chemical agents

	HAV	HBV
1-Survive in	i.**H_2O & sewage** for long periods ii.At **4C**	i.**Dried blood** for ws ii.**Environmental surfaces** for 7 days at 25C
2-Resistant to	i.Heat at 60C for 1 hr ii.Extremes of pH:3(gastric acidity) ***iii.Lipid solvents (70% ethanol)***	i.Heat ii.pH
3-Susceptible to	i.1% Na hypochlorite &2% gluteraldehyde	
		ii.Ethanol (70%) iii.Heating at100C for 1 hr or autoclave

	HAV	HEV
Family & Structure	*1-Picorna* viruses : Hepatovirus genus	Related to *Calici* viruses
	2-SS RNA : + ve sense 3 - 1 serotype	
	4 – Capsid : icosahedral 5-Non eneveloped	
Modes of transmission	**Feco-oral** : ingestion of contaminated food & H_2O (not by blood due to low viremia)	
Pathogenesis		***Water -borne*** epidemics
A - Entry & spread	**1-Ingestion** → 1ry multiplication in *GIT*	
	2- Spread by blood to liver → Multiplication in hepatocytes	
	3-No CPE : infected cells are damaged by *CTLs*	
B - Fate	**1- Clearnace of inf.** → repair of damage & recovery	
	2-NO : chronicity,carriers or carcinoma	
		High mortality in ***pregnant*** ♀
Immunity	✓ **IgM** : Onset of jaundice	
	✓ **IgG** : 3ws later → lifelong imm.	
Cl.picture	**Infectious** hepatitis	**Enteric Non A non B** hepatitis
A-IP	2 ws (Most inf. are asymptomatic)	
B- S & S	Jaundice,dark urine&pale stools (***Children*** are the most frequently affected)	
Treatment	No antiviral drugs	
Laboratory diagnosis	**I- Non specific tests :** Marked ↑ in liver enzymes & bilirubin	
	II- Detection of Abs in serum by ELISA	
	1.IgM indicates recent infection	
	2.IgG indicates past infection	
	IgG may indicate vaccination	
	C - RT-PCR : detects viral RNA	
	D – EM : Detects virus in stools	
	E – RIA : Detects viral Ag	

Prevention of hepatitis viruses

I - Hygenic measures (behavior modification)

HAV & HEV

Most important

1-Good hygiene

2-Chlorination of H_2O

HBV & HCV

1-Avoid parentral transmission by

- **Proper exam. of blood&** blood products
- **Proper sterilization &** standard precautions
- **Avoid sharing** of needles&razors
- *No blood from any pt* ***with hepatitis history***

2-Ceserian section : for chronic carrier pregnant ♀

II – Immunization

HAV

HBV

A - Active : vaccine

1 - Preparation & administration

Inactivated

♣ IM: 1st dose

↓ 6ms

2nd dose

♣ ***S Ag*** *produced in yeast by* ***recombinant technique***.

♣ **3 doses** :0,1&6ms

♣**IM** : i. *Deltoid* : Children & adults *ii.Thigh* :newborn

2 - Indications

Children

i.Routinely to newborns& adolescents

ii. High risk groups(frequently exposed to blood&blood products)

- ♦ Hemophilia
- ♦ Hemodialysis
- ♦ Health care workers
  - •Dentists •Surgeons •lab.workers

B - Passive : Post exposure prophylaxis

HAV Igs

1- HBV Igs (anti S)

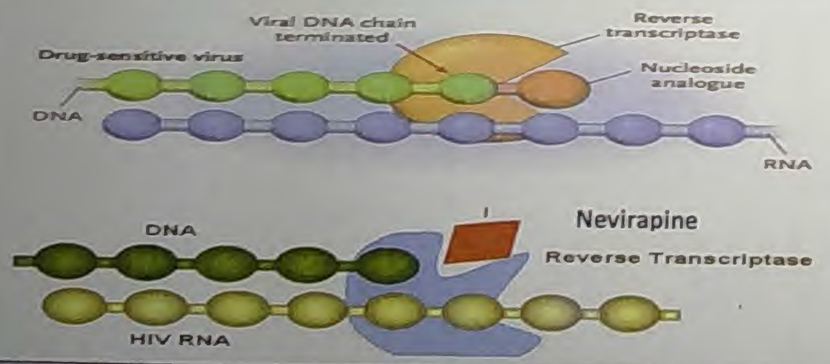
Accidental exposure ***to S Ag+ve blood :*** Needle prick or sharp injury

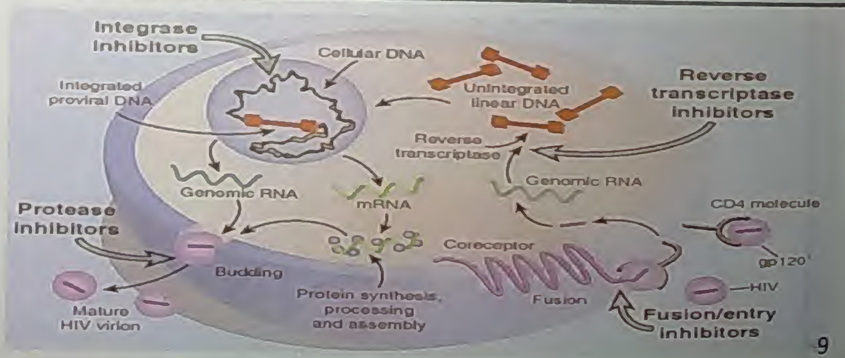
Newborn ***to S Ag +ve mother***

2- Vaccination is given simultaneously at a separate site

Antiviral chemotherapy

Mechanism of action	Examples	Uses : TTT of
I-Drugs affecting attachment&penetration (Fusion inhibitor) Blocks fusion between virus & CM	Fuzeon	*HIV*
II-Drugs affecting uncoating Blocks virus uncoating	Amantadine & Rimantadine	Prophylaxis & ttt of influenza A
III-Drugs affecting nucleic acid synthesis		
1-Nucleosides analogues ⊖ DNA polymerases → ⊖ NA replication	Acyclovir ♦ Gancyclovir	•*HSV&VZV* ♦ *CMV*
2-Reverse transcriptase (RT) inhibitors i.Nucleosides analogues : ⊖ synthesis of proviral DNA ii.Non nucleosides analogues: binds directly to RT	• Azydothymidine (AZT) & Dideoxyinosine(DDI) [less toxic] ⋆ Lamivudine ✓ ♠ Nevirapine	•*HIV* ⋆ *HIV & HBV* ♠ *HIV*
3- Interference with mRNA *(Both DNA&RNA Viruses)*	Ribavirin	*HCV &RSV*
IV-Protease inhibitors ⊖ viral protease required at late replication to form mature virion → Non infectious virus	Indinavir	*HIV*
V-Drugs affecting release: ***Neuraminidase inhibitors*** ⊖ virus release from infected cells ➡ ↓ viral spread &limits inf.	Zanamavir & oseltamivir (inhalation) (oral)	*TTT ofInfluenza A&B viruses*





Virology 4

Enveloped RNA

Enveloped RNA viruses

Respiratory			Zoonotic		Retroviruses
Myxoviruses	**Rubella**	**Corona**	**Rabies**	**Arbo**	**HIV**
Local or systemic	♦ Systemic ♦ Congenital	Local			

Myxoviruses

(**Myxo** = affinity to **mucin**)

	Orthomyxoviruses	Paramyxoviruses
1-Members	**Influenza** V : local	**i.Parainfluenza**V & **Respiratory syncitial** V: local **ii.Mumps** V & **Measles V**: Systemic
2-Size	Smaller	***Larger***
2-RNA genome	***Segmented***	Non segmented
3-Genetic reassortment& **Antigenic variation**	***Very common***	Very rare

Influenza Viruses

Structure , Ags & Classification (1)

A - Nucleocapsid

Genome
SS RNA ↔ **Segmented**
-ve sense — ***8*** segments

Shape
Helical

Ags & Classification
2 type specific protein Ags (core Ags)
Nucleocapsid Ag & ***Matrix (M)*** Ag → Divide V into *3 serotypes: A,B&C*

B - Envelope

Contains 2 projecting glycoprotein spikes : HA&NA

1-Classification

Subtype (strain) specific Ags (Major Ags) → Divide **type A** into strains → Each one is named according to ***its type of HA &NA***
e.g H1N1&H3N2 (there are *16 H &9 N*)

2-Functions

Heamagglutinin (**HA**)	Neuraminidase (**NA**) (2)
1-Binds to host cell **receptors** → viral ***entry***	1- Cleaves **neuraminic acid** of infected cell → viral ***release***
✓ Abs against it ***neutralize infectivity & prevent ds***	❖ Its Abs ↓ **viral release &spread** → **reduce ds**
2-Heamadsorption & Heamagglutination of animal RBCs	2-Degrade **protective mucin** in RT → Binding of HA to receptors

Antigenic variation

	Antigenic drift (3)	**Antigenic shift** (4& 5)
1-Type	Type **A & B**	Type ***A only:*** **Wide host range** ; infects both human & animals: Pigs,aquatic birds & chicken
2-Etiology	Spontaneous **point mutation**	***Genetic reassortment :*** 2 viruses of **different strains** infect a **single** cell (In pigs : susceptible to avian,human &swine strains) ↓ **Gene** segment coding for **HA** or **NA** in **one** strain is replaced by ***another seg.*** from the ***other*** strain
3-Result	**Minor change** in a.a.squence of **HA** or **NA** → **Annual change** of vaccine	***New*** strain with ***new HA or NA*** ↓ No one is immune as *it isn't covered* by *annual vaccination* → ***Epidemics & pandemics***
4-Time	**Ongoing** : every yr or few yrs	Every ***10-20 yrs***

Types of Influenza virus

	Type A	Type B	Type C
1-Host range	Human & animals.....	Only human	
2-Agenic variation	Shift & drift	Drift only	Stable
3-Severity	Severest Epidemic & pandemic every 10-20 yrs	Less severe Outbreaks only	Doubtful pathogenecity

Avian Influenza virus in humans

I-H5N1

Pathogenesis & Outbreaks

Infect chicken & other birds more effectively than humans (Why?)

- Viral receptor is present throughout the chicken RT → Primarily cause avian influenza in chicken
- Viral receptor in human is present only in alveoli
  - Humans are rarely infected
  - *Extensive exposure* → Virus can reach alveoli → *Severe pneumonia* → High mortality rates in 1997,2003-2004

Mode of transmission

- **Direct spread from chicken**
  By respiratory secretions& guano
- **Rare human to human spread**
  Can ↑ dramatically *if reassortment with human strains occurs*

II-H7N9

Outbreak was restricted to China

Swine Influenza virus in Humans : H1N1

Pathogenesis & Outbreaks

- Outbreaks of human influenza in 2009 *(No previous outbreaks in pigs)*
- Arise from reassortment of swine, birds & human genes
- Human to human spread
  Affect mainly young people (≤ 18yrs)
- Mild symptoms & Few fatalities in IS pts
- No Abs against swine HA in most people

Modes of transmission of Human influenza (Highly contagious)

- **Droplet**
- **Airborne**
- **Contact** :direct & indirect

Pathogenesis

- **NA** degrades **protective mucin** layer over epithelial cells of RT
  ↓
  Virus ***attachment by HA***
  ↓
  Damage of cilia & desquamation
- Infection is **limited to RT**
  as ***local EC proteases modifies HA***
  to become *active*
- **Systemic symptoms**
  are due to ***cytokine*** *release*
  (viremia is rare)

Cl.picture

- **Local**
  ♦Nasal discharge
  ♦Dry cough
- **Systemic**
  ♠Fever,headache
  ♠Myalgia
- **50%** of infected people are **asymptomatic** but **contagious**
  ↓
  Difficult to stop ds spread

Complications

1-Pneumonia

1ry influenza
(Fatal)

✓ **2ry bacterial**
(most common)
- ☻ *S.aureus*
- ☻ Pneumococci.
- ☻ H.influenza

2-Rye syndrome (rare)

♣ Encephalitis & Hepatic necrosis
Following ***Salicylate*** intake

♣ Causative virus
- *Influenza A&B*
- VZV

♣ Age
Children& adolescents (***2-16 yrs***)

♣ Prevention
Avoid salicylate in children *with **flu-like symptoms***

Prevention & control by vaccines

Quadrivalent vaccine : most recent isolates of **H1N1,H3N2 + 2 B strains**

→ Reformulated every year to contain current antigenic strains

I-Killed vaccine

A-Prep.& Administration

Killed vaccine in **chick embryo**

IM or ID

B-Indications

Persons with ↑ risk to develop complications & their contacts

i.Extremes of age ii.Elderly people iii.IS pts iv.HCP

C-Effect & Administration : *Short lived protection due to*

Short lived immunity

Given in **the fall**

High protection in Dec/ Jan (peak months)

Change of strains due to **shift &drift**

Given **every year** (may be changed)

based on worldwide monitoring of influenza

II-Live attenuated

Preparation

Temperature sensitive mutants

Can replicate in ***cold nose (33C)***

No replication in **lower RT (37C)**

Administration & effect

Nasal spray

Mucosal,

humoral & CMI

Indications

Healthy individuals with no risk for complications

III - Recombinant Vaccine

Inserting the ***gene coding for HA*** in a vector

- Both inactivated & live attenuated vaccine become available **against swine flu in 2009**
- There is ***no human vaccine for H5N1***,but there is one available for avian species

Prevention & Treatment

	Amantadine &Rimantadine	Zanamavir & Oseltamivir
1-MOA	⊖ ***penetration*** & ***uncoating***	⊖ ***neuraminidase*** → ↓ viral spread → ↓ duration of symtoms
2-Uses & Indications	**Ttt & prevention** of type **A** only • Swine & avian flu are resistant Vaccine is preferred for prophylaxis	**Ttt** only of type **A & B** (*swine &avian flu are sensitive*) ♠ ***Post exposure prophylaxis*** in non vaccinated elderly Must be taken within 48 hrs of symptoms

Paramyxoviruses

General Characters

A-Nucleocapsid

- **Genome**
  - SS RNA:-ve sense
  - *Unsegmented*
- **Shape**
  - Helical
- **Nucleoprotein Ags**

B-Envelope : Contains 2 **specific glycoprotein** projections

1-Haemagglutin-Neuraminidase (HN)

- **Function**
  - *Attachment of virus*
  - Haemadsorption & Haemaggl.
- **Lacks neuraminidase activity**
  - In measles virus
- **Absent in**
  - Respiratory syncitial V.

2-Fusion (F)

Promotes **fusion** of

- *Host &virus CM* → **Infection**
- *CM of* ***infected host cells*** → **Syncitium**

C-Antigenically stable

D - MOT : Respiratory secretions ; droplet & contact

Respiratory syncitial virus (RSV)	Human parainfluenza viruses 1,2,3&4 (HPIV)
Virus structure	
1-Nucleocapsid (E)	
2-Envelope	
F only (E)	HN & F (E)
Pathogenesis &Cl.P	
1-Upper RT ds : *common cold* like symptoms (repeated attacks)	
2-Lower RT ds : *Pneumonia & bronchiolitis*	
i.Especially in **elderly:** Pts with heart,lung & immune deficiency ds ii.Very common in **infants < 1 yr of age**	
The most common cause	The 2nd most common cause
	3 -Croup (laryngotracheobronchitis) : by HPV1&2
Treatment	
•O_2 •Mechanical **ventilation** •**Ribavirin** aerosols	

Systemic Viruses

	Mumps virus	Measles virus	Rubella virus
Family	**Paramyxoviruses**		**Toga virus**
Structure			
1-Nucleocapsid			
2-Envelope	E		SS RNA **+ve** sense
	E		2 glycoproteins ***1 Heamagglutinates RBCs***
S & MOI	❖ **Respiratory secretions & saliva** :droplet and contact		
	✓ ***Urine***	✓ ***Airborne*** ♦ Highly contagious ♦ Maximal infectivity before rash	✓ The only Toga virus not ***transmitted by arthropods***
Pathogenesis &Cl.P	**Epid. non sup. parotitis**	**Measles (rubeola)**	**German measles(post natal rubella)**
A-Age affected	5-15 yrs	Younger age	As mumps
B-Initial replication & viremia	**1-Nasopharynx**	**1-Upper & lower** RT	
	2- Regional LNs → **viremia** → spread to multiple tissues		
D - Affected tissues	**1-Glandular tissues :** •Salivary glands ***Parotitis***  •Pancreas •Testes & ovaries •Thyroid **2-Meninges** ***Aseptic meningitis*** *(mild)*	**1-Conjunctiva : *Conjunctivitis*** → photophobia **2-Oral cavity : *Koplick's spots*** •**White dots** inside cheek  •Before rash & **disappear** after its onset **3-Skin : *Maculopapular rash*** **Etiology** ↔ **Site** ***T cells attacking VIECs*** in small BVs ↔ ***Face*** Palms & soles Exfoliation after **7** days 	**1-Cervical LN ++** Suboccibital & postauricular  **2-Skin** ***Maculopapular rash*** **Face** → *trunk* → *extremities* **Disappear** after **3** days 

	Mumps	Measles	Rubella
E-Immunity	1 serotype causing systemic inf. → *Long* lasting immunity by *neutralizing IgG*		Repeated attacks may occur
		Maternal Abs protect infant for 6-8 ms	
Complications	1-Glandular tissues ☺ Orchitis → Sterility in adults ☺ Oophritis ☺ Pancreatitis ☺ Thyroiditis 2-Severe aseptic meningitis In adults	1- Pneumonia *2ry bacterial pneumonia* (Most common) ↔ *Viral giant cell pneumonia* (rare but fatal) With ↓ CMI	
		2-Neurological (rare)	
		a.Postinfectious encephalitis *Few days* after the rash disapspear	b.Subacute sclerosing panencephalitis *10 yrs* after initial inf	Postinfectious encep. *1w* after rash → Recovery with no sequelae

Prevention

I-Active immuniz.			
	A- Monovalent vaccine		
1-Preparation	Live attenuated → given SC		
	In *chick embryo*		In *human diploid cell culture*
2-Effect	Long term immunity		10 yrs immunity
3-Indications		i.Routinely to **children**	
			ii.Non pregnant adult females → Avoid pregnancy for 3ms
	B - M M R vaccine		
1-Preparation	3 **live attenuated** viruses → SC 2 doses *a.1st* : children at **12 ms** (no strong IR if given earlier) *2nd* : at **4 yrs** (or 4 ws after 1st)		
2-Contraindications	*i.IS pts* *ii.Pregnant* ♀		
II-Passive immunization		By human Igs Within *1 w of exposure* to inf. i.IS pts, ii.Pregnant ♀ { (vaccine is contraindicated)	

Congenital rubella syndrome

Mode of transmission & pathogenesis

Maternal viremia (1ry inf.) during pregnancy

↓

Infection of fetus

↓

↓ fetal cell growth rate without destruction

↓

Hypoplasia of organs

↓

Extent of teratogenic effects depends on **timing of fetal infection**

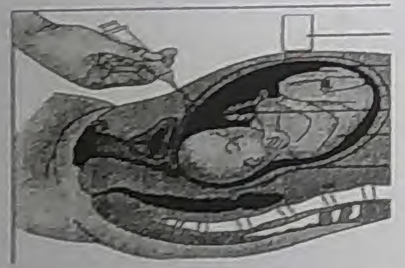
- In 1st ***18 ws*** → ***most critical***
- After 18 ws → Uncommon defects

Cl.P

- **Transient symptoms**
  - Growth retardation
  - Anemia
- **Permanent defects**
  - Microcephaly
  - *Cataract*
  - *Deafness*
  - Congenital heart ds

Laboratory diagnosis

A-During pregnancy



1st : Confirm ***recent maternal rubella*** infection by **ELISA**

- Ig*M*
- ***Rising titer*** of Ig*G* in 2 samples

2nd : Confirm **fetal affection** by **DIF** : Detect ***Ag in amniotic fluid***

→ **+ve** results in **1st trimester** → therapeutic **abortion**

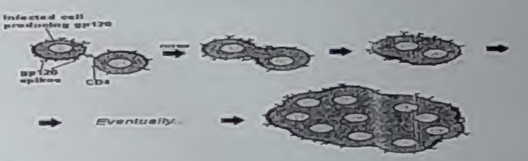
B-After birth

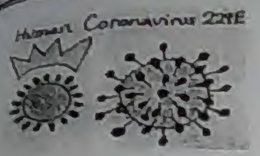
- **Live newborn** : by **ELISA**
  - Detection of *antirubella IgM* in serum
- **Still birth** : **virus detection** from organs
  - Culture on **MKTC**
    - Rubella virus *interferes* with *CPE* of ***Coxsakie*** or ***ECHO***
  - **DIF**
    - Detection of viral Ag

Prevention & Control

- **Vaccinate women in**
  - ***School*** age
  - ***Childbearing age*** Avoid pregnancy for 3 ms
- **Therapeutic abortion in 1st trimester**
  - If ***recent*** maternal infection &fetal affection are ***confirmed***

Laboratory diagnosis of Myxoviruses

	Influenza V	HPIV	Measles	Mumps	RSV
I-Specimen	Nasal aspirate			**Saliva , CSF**, urine	Nasoph.aspirate
II-Direct detect.					
A-DIF	Detects viral **Ag**				
B-RT-PCR	Detects viral **R N A**				
III-Isolation					
A-Culture	**Monkey kidney tissue culture**				**Hela cells**
B-Recognition of growth	**♦Haemadsorption**				NO
	NO	♦*CPE* → *giant cell* 			
		♦Intranuclear & Intracytoplasmic IB 	NO		+ Syncitia
C-Serotyping by HIT	Add specific ***monoclonal Ab*** to identify ***serotype***	NO			
IV-Serology	**ELISA** 1-Ig***M***2-***Rising titer*** of Ig***G 4*** folds in 2 samples (most important)				**ELISA**



Corona Viruses

Structure

- **Genome**: SS RNA+ve sense ↔ largest RNA genome
- **Capsid**: Helical
- **Envelope**: Has club-shaped projections → crown or solar corona-like

Mode of transmission

- Inhalation of droplet aerosols
- Close contact: touching or shaking hands
- Feco-oral

Clinical picture

Respiratory diseases				Enteric diseases : enteritis in neonates
Common cold	***Bronchitis***	***SARS***	***MERS***	Destroys epithelial cells **(as Rota V.)**
2nd most frequent cause after Rhino V				Loss of absorptive capacity of enterocytes

	SARS(Severe acute respiratory syndrome)	MERS (middle east resp.synd.)
1-Virus	SARS CoV (mutant corona)	MERS CoV (new corona)
2-NR	Bats	
3-Origin	China 2002	Saudia Arabia 2012-2013
4-MOI	Airborne	Direct or indirect contact with camels in SA,Qatar&Egypt.
5-Receptor	***Angiotensin converting enzyme-2*** on respiratory epithelium → Dysregulation of fluid balance → Edema in alveolar space	**CD26** on respiratory mucosa (not ang.conv.enz.)
6-Pathog.	*1-Cytokine storm* in blood for 2ws. 2-Virus is detected in liver,kidney&SI 3-Leukopenia & thrombocytopenia	
7-Cl.P	**1-Atypical pneumonia** : (interstitial ground glass infiltrate in X rays) non productive cough, fever(38C),dyspnea&hypoxia **2-Acute respiratory distress** → Acute respiratory failure (10%)	Fatal pneumonia (outbreak)
8-Treatment	*a.No specific antiviral ttt.* b.Support vital organ functions in severe cases	
9-Prevention	a.Infection control precautions *b.No vaccine*	

Laboratory diagnosis

- **Common cold**: Clinical
- **SARS & MERS**: ***1-Ab*** in serum ***2-RT-PCR*** in resp.secretions
- **Diarrhea**: 1-RT-PCR **2-EM**

Retroviruses

Characteristic feature (	Members of medical importance	
They have **a reverse transcriptase enzyme** that converts viral RNA into DNA (6) → Integration into host DNA → Lifelong infection	HIV • Slow • Cidal • Non oncogenic	HTLV 1 Oncogenic

Human Immunodeficiency Virus (HIV)

Classification

- *2 types : HIV -1 & 2*
  - **Same** Cl.picture
  - **Type 2** — ***Slower*** progression — Only in ***West Africa***
- Each type ***mutates rapidly*** — *Difficult ttt or vaccine*
- Each type has ***many subtypes***

Structure (7)

I - Internal structures

A-Nucleocapsid

- **SSRNA** — *+ve* sense
- **Diploid** — *2 identical* RNA copies per virus
- **Genes** — *Encodes important proteins*
- **Capsid** — *Cone-shaped*

B-Internal proteins

A- 3 enzymes → Integration & Replication of virus			B- Structural protein
Protease	***Reverse transcriptase***	***Integrase***	**P24 : *Most abundant*** core protein
Cleaves viral precursor proteins into *functional proteins*	Converts SS RNA into *DS DNA*	*Inserts Ds* DNA (provirus) into host chromosome	Detected during early infection *Indicates vial replication*

C- Other proteins

- Enhance viral transcription
- ↓ expression of MHC class I

II - Surface glycoproteins

- **GP 120 : Major Ag** on the surface — *Binding of CD4 mol.on Th*
- **GP41:** transmembrane — Fusion of envelope with Th CM

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Pathogenesis of HIV

I-Tropism

CD4 + Th cells are the 1ry target of HIV

Certain subsets of monocytes express CD4 mol

II-Attachment & Entry into CD4+ cells (8)

GP120 binds to **CD4** mol.on target cell

Binds to coreceptor (*chemokine receptor*) :

CXCR4 on Th or **CCR5** on MQ

↓

GP41 fuses viral envelope with target **CM** Entry of virus contents & infection

Mutation of genes encoding for **chemokine receptors**

→ protection from inf.with HIV

C-Replication in CD4+ cells & Release (9)

Reverse transcriptase converts RNA into *DNA which is transported to nucleus*

↓

Integrase *inserts* DS DNA (provirus) into chromosome

↓

Host cell polymerase *transcribes* viral gene into viral mRNA

↓

Translation into viral proteins & replication of viral genome

↓

Processing of capsid proteins **by viral protease** &Viral assembly & release by budding

↓

Infection of new target cells

D-Fate of infected cells

Killing of CD4 Th infected cells	Reversion of Th to a resting memory state	Monocytes
1-Direct killing : Large amounts of viruses are produces & buds off from cell surface **2-Apoptosis** : Distortion of cell regulation by accumulation of viral proteins & NA **3-CTLs**	A fraction of infected CD4 Th cells survives ↓ **Long term stable reservoir of virus**	Are relatively refractory to CPE of HIV ↓ Survive &harbor large quantities of virus **i.Disseminate the virus** to lung & brain ii.Continue to produce virus for long period

E- Mechanisms IR evasion by HIV

1-Integration of viral DNA in host cells

persistent infection.

2-High rate of mutation in genes coding for env.glycoproteins

3-Down regulation of MHC class I required for CTLs to recognize infected cells

Treatment

I-Immunotherapy

- Mc Ab against GP 120
- Soluble CD4 mol.

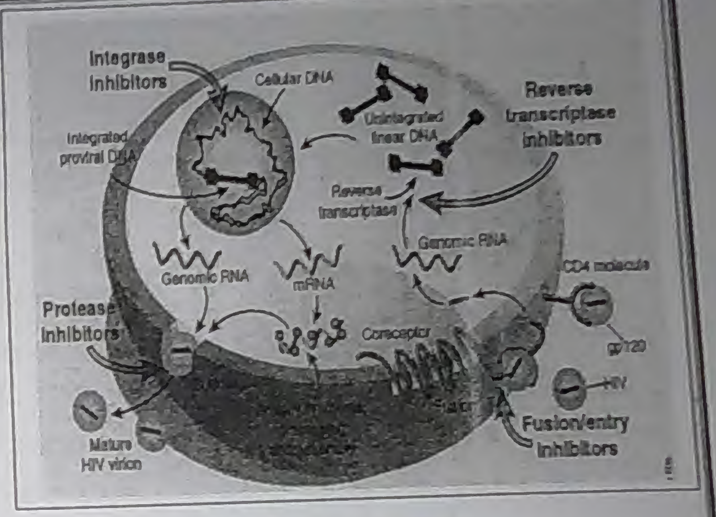
II - Antiretroviral drugs

A-Aim

Suppress ***HIV replication***,but ***don't eradicate*** the virus (no cure)

↓

Protection of IS



B-Modes of action

- ⊖ **Fusion** to lymphocytes
  - *Enfuvertide*
- ⊖ **RT**
  - Nucleoside **analogues**
    - ♦*Azydothymidine (AZT)*
    - ♦*Dideoxyinosine (DDI)*
  - **Non** nucleoside **analogues**
    - *Nevirapine*
- ⊖ **Integrase**
  - *Raltegravir*
- ⊖ **Protease**
  - ⊖ assembly & budding
  - *Indinavir*

C - Combination HAART (Highly active antiretroviral ttt) regimen

2 nucleoside analogues + **Protease** ⊖

↓

Avoid development of resistance due to *high mutation rate* of HIV

D-Monitoring of ttt : By measurement of

- ***Virus*** load
- ***CD4+*** cells

III - Antibiotics : for oppurtunistic infections

Disinfection & Inactivation

- ***10% Na hypochlorite&70% ethanol*** on contaminated surface for 10 min
- ***Heating at 56C*** Inactivates the virus in liquid
- ***Exposure to undiluted bleach for 30 sec*** If the virus is present in clotted or unclotted blood in a needle or syringe

Clinical picture : 3 stages (10)

	Early acute : 2-4 ws after infection	Middle latent	Late
A-Virological features	**1-Early** ***a. High viremia:*** i.Spread to many regions including lymphoid tissues & brain ii.Most infectious stage 2- **Later on** ***a-Low level viremia*** **b. *Virus reaches set point*** Represents the amount of virus produced & remains constant for yrs (differ between pts) → The higher the set point,the more likely the progression to symptomatic AIDS	**HIV continues to replicate in lymphoid organs** ↓ Large amount of virus is produced by LN cells & remains sequestered in LNs	**Collapse of LN architecture** ↓ **Loss** of IS ability to **trap HIV** or other infectious pathogens ↓ ***Viral load ↑*** in peripheral circulation
B-Clinical features	*1- **Inf.mononucleosis like symptoms(90%)*** a.Fever,sore throat & LN enlargement b.Maculopapular rash on trunk &extremities ***2- Asymptomatic (10% of cases)***	•**Asymptomatic** •Lasts 7-11 yrs	• **Long lasting fever** (1m) •Weight loss• Fatigue •↑severity of opportunistic inf.
C-Immunol. Features	**1-CD4 + count** **a. Early :** ↓ significantly **b.Later :** *revert to normal by :* ↑ CD8+ cells & Ab against HIV 2- **Seroconversion :**Detection of Abs in serum ♦Usually 1-4 ws after infection ♦**May be delayed up to 6 ms :*Window period*** No Abs are detected although the viral load is high	**Early : Immune competence** Generation of ***new*** CD4+T cells *compensates destroyed ones* ↓ **Immune surveillance** prevents most of infections	♦**CD4 + count ↓ to < *200 cells/* mm³** (The lower normal limit is ***500 cells/*** mm³) ♦The 2 characteristic manifestations of AIDS are **Pneumocystis carinii & Kaposi sarcoma** ♦ **Other opportunistic inf.** *a.Bacterial* : Listeria M.TB, M.avium intracellulare *b.Viral :* CMV,HSV&VZV. *C.Fungal :* Candida,Cryptococcus

Pediatric AIDS

In neonates, viral RNA ↑ rapidly in 1st few ms of life & **doesn't ↓ rapidly as in adults** as the IS is immature

The level of RNA predicts the rapidity of progression to AIDS

Signs of AIDS can appear **early by 5 ms** (80% of cases)

Laboratory diagnosis

A-An initial HIV screening test : either by

1-Ab tests : Detection of Abs for both HIV 1&HIV 2 Ags.

2-Ag/Ab test : detection of Abs & P24 Ag

B-Follow up testing : performed if the initial result is +ve

1-Ab differentiation tests : distinguishes HIV1 from HIV2 tests

2-Qualitative &Quantitative detection of HIV nucleic acid:

Performed if the initial HIV screening tests are +ve

a. Detects initial baseline viral load (set point) ⟶ Predicts time of AIDS onset

(↑ set point⟶ faster AIDS onset)

b.Prognostic marker after initiation of ttt.

C-CD4 cell count

(The lower limit of normal CD4 count is 500 cells/mm3)

↑opportunistic inf.when CD4 count ***falls < 200 cells/mm3***

⬇

Determines whether a pt **needs chemoprophylaxis** against opportunistic inf.:

Diagnosis of HIV inf.in newborns & infants

RT-PCR : detects viral RNA

❖ ***Ab detection isn't useful***

Transferred maternal Abs are present up to 18 ms

whether the newborn is **infected or not**

Modes of transmission

A-Sexual route : Main route

Virus is present in **semen** & **vaginal** secretions

- *Male homosexuals (commonest)*
- Heterosexuals

B-Blood or blood products route

- Blood transfusion
- **Needle stick injuries**

The risk of percutaneous exposure is **0.3%** (High infectious dose of HIV)

C-Perinatal route

- Transplacental
- At birth
- Breast feeding

Prevention & Control

General Measures

As HBV (E)

Vaccine : under trials &is **hindered** by

- Rapid ***mutation*** in ***Env*** region
- ***No*** viral ***exposure*** to ***Abs*** (Spread by fusion)
- ***No animal models*** for AIDS

Post exposure prophylaxis after needle stick injury from HIV positive pts

Risk of getting HIV	Drugs	Follow up by HIV testing
Very low (< 1in 100 exposures)	Anti HIV drugs within 72 hrs → 28 days ↓ replication of HIV&its spread	At 6ws ,3ms & 6ms

Human T cell lymphotropic virus 1 (HTLV-1)

MOT

- Sexual
- Blood transfusion
- Contaminated needles(IV drug users)
- Breast feeding

Pathogenesis & Ds production

On mature T cell: ***Oncogenic & non cidal***

Viral RNA RT→ DS DNA → integration into chromosome → ***Adult T leukemia-lymphoma***

On nervous system

Degeneration → ***Spastic paraperesis***

Laboratory diagnosis

RT-PCR: Detects viral RNA

ELISA : Detects Abs

Rhabdo Viruses : Rabies virus

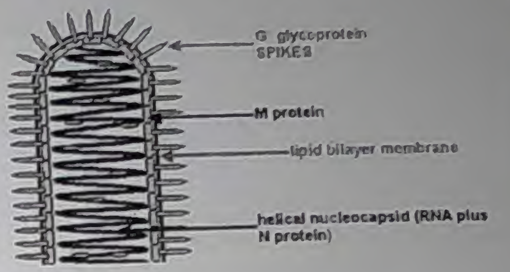
Structure

A-Nucleocapsid

ss RNA : -ve sense — Helical — ***Bullet*** shape

B-Envelope

Has **glycoprotein** projections → viral **entry** → target of **neutralizing** Abs



Host range : Broad

Infects all mammals → Lethal acute encephalitis

Modes of transmission & Animal reservoirs

1-Bite of rabid animals : virus in saliva of

Dogs ,cats & wolfs : main reservoirs

Aggressive behavior due to encephalitis

Bats

Healthy

2-Corneal transplantation (very rare) **:** from infected *cadaver*

3-Airborne aerosols in : bat *caves* & *laboratory* work

Pathogenesis

1-Virus multiplies in striated muscles at site of bite

Invades sensory neurons

Retrograde axonal transport

Reaches **spinal cord & brain** → multiplication

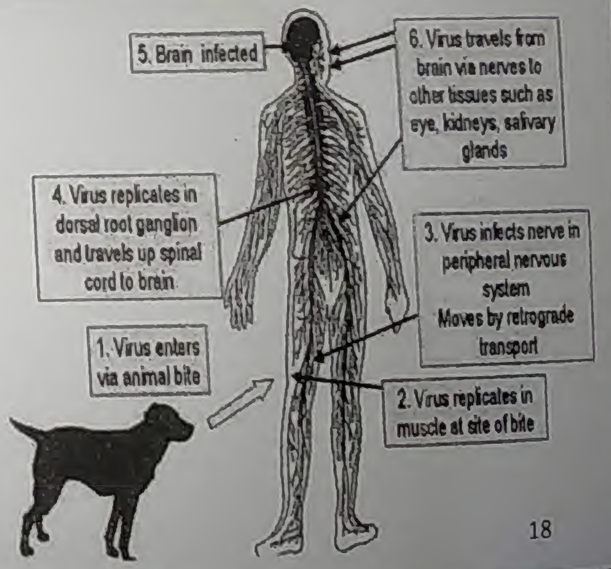
Encephalitis — Neuronal death — ***IC Negri bodies***

2-Virus migrates via peripheral nerves

Salivary glands → *saliva* → transmitted by bite — Eye,skin & Kidneys

3- Viral replication is restricted to neuronal tissues with no viremia

Virus is protected from IS → No or little IR



Cl.picture

A-IP : 4-12 ws

Shorter with bites in *head & neck or in children* — Longer with bites in limbs

B-Phases

1-Prodrome of non specific symptoms : Fever ,anorexia & change in sensation at the site of bite

2-One of 2 forms : death is inevitable

Furious rabies : 80% of cases	*Paralytic rabies*
Brain is involved • Excitement,seizures •**Hydrophobia** : fear toswallow due to painful spasms of swallowing muscles	Spinal cord is 1rly involved ♠ Ascending paralysis & respiratory failure

Laboratory diagnosis

Rules

No laboratory tests to diagnose human inf. after exposure to bite & before appearance of symptoms

Several tests are necessary for antemortum diagnosis (no single test is sufficient)

A - Direct virus demonstration

Saliva,spinal fluid &Skin biopsies of hair follicles at the nape of neck

DIF: Viral Ag

RT-PCR : Viral RNA

B-Isolation of virus

Saliva, CSF or urine

Intracerebral inoculation in mice → Encephalitis → Examine brain for Ag & **Negri bodies**

On human diploid cell culture

C-Serology : IIF

Serum & CSF **Abs** appear **late** during ds progression

Post mortum diagnosis

Detection of Negri bodies in brain or spinal cord by L/M

Management of rabies

General rules

- Immediate washing of wound with soap & H_2O
- *Early post exposure prophylaxis*: •Vaccine • ± Igs
- Tetanus immunization
- No wound suturing before local Ig inflitration

Post exposure prophylaxis

A-Unvaccinated or vaccinated from > 5 yrs or Incomplete vaccination

RIG + vaccine for both bite & non bite exposure (regardless of time interval between exposure & initiation of PEP)

Rabies Igs (RIG):Human or equine

1 dose IM on day **0** & up to day 7

Most into & around wound ↔ Rest in gluteals

Rabies vaccine

5 doses: 1 ml IM Days :**0, 3, 7, 14 & 28**

Important rules

Discontinue PEP if the animal was captured & proved to be ***non rabid by DIF***

Any one coming ***into contact*** with CSF,,saliva or MM of ***suspected person*** should receive ***complete prophylaxis***

B-Completed the schedule of vaccine within last 5 yrs

2 doses (1ml) of vaccine IM : days 0&3

Rabies vaccines

Human vaccines : *Inactivated cell derived vaccines*		
Human diploid cell V. (HDCV): *Gold standard*	**Rhesus monkey vaccine**	**Duck embryo vaccine:** Low immunogenecity

Preexposure vaccination

A-Doses : 3 doses:day **0**,**7**, 21 or **28**

B-Indications : few people

High risk individuals	Traveler's to countries where rabies is widespread if	
•*Veterinary doctors & laboratory workers* •Animal handlers	visiting remote villages where *medical care is difficult to obtain*	*staying > 1 m* in area where rabies is common

Prevention & control

A-Animals

- Eliminate stray animals
- Vaccination of domestic dogs & cats
- Avoidance of wild animals

B-Follow preexposue & postexposure prophylaxis

Arboviruses

(Arthropod- born viruses)

Structure & Classification

100 V infect human

1-Genome	Flavi V	Toga V	Bunya V
2-Envelope	SS RNA + ve sense		SS RNA –ve sense & *segmented*
3-Members	E n v e l o p e d		
	i.Dengue Fever V. *ii.West Nile* fever V. *iii.Yellow* fever V.	*Sindbis* V.	*i.Sandfly* fever V. *ii.Riftvalley* fever V.

General Cl.P

- Most inf.are **asymptomatic**
- **Flu-like**:fever&headache
- Rash,myalgia & LN++

Clinical syndromes

- **General Cl.P**
- General Cl.P +**Encephalitis**
- **Hgic fever**

Laboratory diagnosis

Specimen : blood

- **Direct virus demonstration**
  - *ELISA* — Viral Ag
  - *RT-PCR* — Viral RNA
- **Isolation of virus** — *Intracerebral* inoculation in *mice*
- **Serology** — *ELISA*

Arboviruses causing Fever & Encephalitis

	Arboviruses ds with fever		Arboviruses ds with encephalitis	
	Sandfly Fever	*Sindbis Fever*	*Rift Valley Fever*	*West Nile Fever*
A-Structure & Classif.	**Bunya** V.	**Toga** V.	**Bunya** V.	**Flavi** V.
B-Reservoir	*Human* ← **Vect.**: Phelobotomus papatsii → *Human*	*Bird* ← **Vector** : Culex → *Bird*	*Animal* : cattle,sheep → **Vector** : Culex → *Animal*	*Bird:* crows&migrat.birds → **Vector** :culex → *Bird*
C-MOT	V e c t o r i n f e c t s h u m a n			
			Animal infects human by blood &its products	
	P r e v a l e n t i n E g y p t			
			1st outbreak in 1977	
D-Cl.P	1 - G e n e r a l C l . P			
	2-Neck rigidity & conjunctivitis		**2- Encephalitis**	
			3-Retinitis → blindness ***4-Hgic fever*** (rare)	
E-Prevention	**1 - Vector control**	**2 -↓ exposure to vector** : Protective clothes & insect repellants		
			2-Animal vaccines Live attenuated &killed	

Viral Hemorrhagic Fever

Pathogenesis & Complications

A-Virus spreads from site of entry

Multiplication in *local LNs* → Marked *viremia* → Fever & myalgia

B-Virus ↑ vascular permeability of BVs

↓

Vascular leakage

Skin

Flushing & **peticheal hge**

MM hge & marked bleeding

Conjunctival injection

Coagulopathy

Multisystem organ failure

Hypotension & **Shock**

C-Virus localizes in liver , spleen ,BM, LNs & kidneys → Necrosis

Classification

Flaviviruses		Bunyaviruses		Arenaviruses	Filoviruses
Yellow fever	**Dengue** Fever	**Rift Valley** F	**Hantavirus** ds	**Lassa** Fever V	**Ebola&Marburg** ds
Arbovirus-associated Hgic fevers		***Rodent-born*** Hgic fevers			***African*** Hgic fevers

I - Arbovirus-associated Hgic fevers

Yellow fever	Dengue fever
A - Structure & Family : *Flavi*virus	
	4 serotypes : Den 1,2,3 &4 Infection with **1 serotype** **Life long** immunity to it ***No immunity to others*** Repeated infections are common in endemic areas
B-Reservoir & Mode of transmission (not present in Egypt)	
1-Jungle (Sylvan) cycle ***Monkey***-Vector-***Monkey*** Aedes africanus	**2-Urban cycle** : in towns ***Human*** – Vector-***Human*** Aedes aegypti
	Human –Vector-***Human*** Aedes aegypti
Vector infects human	
C - Cl . P i c t u r e	
1-General Cl.P (E)	
	Classical Dengue fever
2-Severe disease	
	Dengue ***hgic F*** (immunological compl.) & Dengue ***shock syndrome***
a.Hgic manifestations	
Black vomitus	*Skin Hge* : Purpura,thrombocytopenia &shock
b.Jaundice &Renal failure	
D - P r e v e n t i o n	
1 & 2 : as before	
3-17 D vaccine : *Live attenuated* 1 dose **SC** given to **travelers and residents** of endemic areas Immunity for **10 yrs**	

II-Rodent-born Hgic fevers		III-African (non-rodent) Hgic fevers
Lassa fever Virus	**Hanta V associated syndromes**	**Marburg &Ebola viruses**
A-Family		
Arenaviruses	**Bunya** viruses	**Filo**viruses
B-Reservoir		
House rat	**Field** rat	Unknown,**but may be bats**
C-Modes of transmission		
Exposure to ***excreta of infected rats*** (urine,feces)		•***Marburg:*** *Exposure to African green monkeys* • ***Ebola:*** *Direct contact with pt blood or secretions*
♦Direct **contact** &contam.**food** ♦**Human to human contact**	**Inhalation** of aerosols of rodents excreta *(No human to human trans.)*	
D-Clinical Picture		
1- Most inf.are **asymptomatic** **2-Multisystem ds:** Liver,spleen &kidneys	**1-Hgic** fever &**renal** syndrome **2-Pulmonary** syndrome	Both cause same ds 1-Fever,vomiting & diarrhea 2-Bleeding into GIT 3-**Hepatic** affection **4-DIC & shock**
E-Prevention		
Rodent control (difficult to eliminate)		1-Follow infection control precautions 2-No vaccines

F- Lab.diagnosis of Ebola & Marburg

1-RT-PCR: detection of viral nucleic acids **2-Serology** : Rising Ab titer.

3-Virus isolation (extreme care during handling specimen)

G-Treatment of Ebola & Marburg

1-Igs against the virus : has variable results. **2-No antiviral drugs**

Virology 3

Non enveloped RNA Viruses Prions

Oncogenic Viruses Collections

Non enveloped RNA

Picorna Viruses	Reoviruses (Rota viruses)

Picorna Viruses

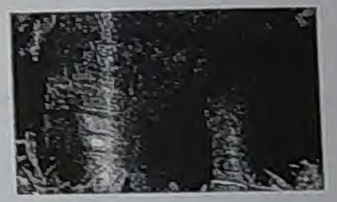
General Structure

- SS RNA, **+ve** sense
- **Capsid**: Icosahedral
- **Non** enveloped
- ***Small***

Members : **4** of **9 genera** are important to humans

- **Entero** V.
- **Rhino** V.
- **Hepato** V.
  - Hepatitis ***A*** virus
- **Aphtho** V.

Aphthovirus of cattle



SOI : Zoonotic

Causes ***Foot & mouth ds*** in cloven-footed animals e.g cattle

MOI

- **Contact**
- **Ingestion** of contaminated food

CL.P

- Fever
- **Salivation**
- **Painful vesicles in**
  - ***Oro***pharynx
  - ***Palms & soles***
  - Fingers & toes

Control

- ***Slaughtering*** exposed animals
- ***Forbid importation*** of infected fresh meat
- ***Vaccination*** of animals

Comparison between Enteroviruses & Rhinoviruses

	Enteroviruses	Rhinoviruses
A-Structure	As before	
B-General characters	1 -Acid **stable** & OT:**37** C 2-Inhabit **GIT**	1-Acid ***labile*** & OT :***33*** C 2-Inhabit ***nose***
C-Classification	***4 members :*** **1-Polio** V. **2- Coxsakie** V. **3-ECHO** V. **4-Other** enteroviruses	***100 serotypes***
D-MOI	**1-Feco-oral (main)** 2-Droplet	**1-Droplet (main)** 2-Direct contact
E-Pathogenesis	**1ry** replication in **oropharyngeal LN & tonsils** Replication in GIT & Peyer's patches Shed into feces ⇠ ***Viremia*** ⇢ into feces Spread to target organs → Symptoms	**Local** replication only in **nasal mucosa** ***No viremia*** Congestion & desquamation of epithelial cells ↑ nasal secretions
F-Disease production	**1-Asymptomatic (most cases)** 2-Fever & rash in children	**Common cold** (most common cause)
G-Complications	***Meningitis*** (rare) Mild encephalitis	***2ry bacterial infection*** Sinusitis &OM ⇠⇢ Bronchitis
H-Immunity		***1-Recovery*** is due to ***IFNα*** 2-Neutralizing Abs in serum & secretions appear late (7-21 days) 3-Local **IgA** & serum **Abs** are **short** lived *Repeated infections are common*
I-Prevention	**Polio** vaccine	**No vaccine** Due to ***multiplicity of serotypes*** with no cross protection

Polio Viruses

Structure : as before

Serotypes & Immunity : 3 serotypes

- Life long immunity to infecting serotype
- **No cross protection**

Clinical picture

A-Asymptomatic polio : most cases

If the virus replicates ***only in GIT***

B-Abortive polio : only in 5 % of infections

- Most common **symptomatic** form
- **Viremia** → Fever, abdominal pain & constipation
- **Neutralizing Abs** develop → ***Recovery***
- Rarely **Progression to NS**

C-Non Paralytic polio (aseptic meningitis) : 1-2 % of infections

- Above symptoms + **Neck stiffness** & pain
- Complete **recovery**

D-Paralytic polio : < 1% of infections

- Virus spreads **from blood** to **AHCs** → Multiplication
- **Pred.F.** *Tonsillectomy* in child with *inapparent* inf. → V.in nasopharynx enters ***cut nerve fibers***
- **Mild lesion** → Nerve cells recover
- **Destruction** of **nerve cells** → ***Flaccid paralysis***
- **Muscle atrophy** → Due to nerve supply affection *(muscle itself isn't affected)*

Reaction to physical & chemical agents

Poliovirus is **inactivated by**

- **Heating** at **55**C for **30** min, but *Mg prevents* this inactivation
- **Chlorine : 0.1ppm** for drinking water

Prevention & Control

I - Active immunization

Oral polio vaccine (OPV) : Sabin	Inactivated polio vaccine (IPV) : Salk
A-Contents & Preparation	
3 serotypes grown on **MKTC** → **3** doses given at 2 , 4 & 6 ms	
B-Effects	
Induce **systemic Abs** : IgG&IgM → *neutralization* of virus → *Protection* of CNS from *wild* virus (100%)	
C- Advantages : Live attenuated	**C-Disadvantages : Killed** (by formalin)
1-Booster dose at 4-6 yrs	**1-Repeated booster** doses
2-Oral → Multiplication in intestine → **sIgA** → GIT protection	**2-IM** → No ……
3-Production of herd immunity Attenuated virus passes in stools of vaccinated children Infects ***non vaccinated*** children	**3-NO**
D-Disadvantages : Live attenuated	**D- Advantages : Killed**
1-Contraindicated in **immunodeficient individual**	*1-Mainly used in* ***immunodeficient individual***
2-Interference Its *replication & immunity is interfered* if **another entero V.** is **infecting** the **gut** of the child Not given to a feverish child	***2 - No interference***
3-Must be stabilized by $MgCl_2$ Prolongs its potency at 4 C (for 1yr) & 25C (for ws)	***3-Stable***

II-Passive immunization

Igs given shortly before infection to asymptomatic contacts → ***Prevent paralysis*** for ***ws***

III-General measures

Proper sanitation

Avoid tonsillectomy in feverish children

Treatment : No antiviral ttt

ECHO (Enteric Cytopathic Human Orphan) Viruses

Classification : 34 serotypes

Diseases

- **Aseptic meningitis**
- **Fever** :with or without rash

Coxsakie Viruses

Classification : according to effect **on mouse**

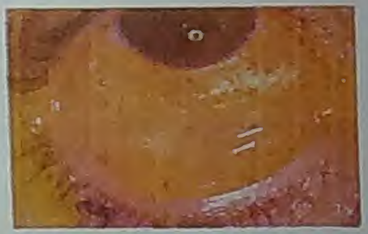
- **Group A : *23*** serotypes
- **Group B : *6*** serotypes

Diseases

1-Both group A & B : a. **Aseptic meningitis** b. **Common cold**

2-Group A

- **Herpangina** : small children
  - ***Pharyngitis*** ↔ ***Vesicles:*** Palate &tongue
- **Hand, foot &mouth ds**
  - ***Pharyngeal ulcers*** ↔ ***Vesicles:*** Palms & soles
- **Hgic conjunctivitis**



3-Group B

- **Pleurodynia** (epidemic myalgia)
  - ***Unilateral*** severe pain in ***intercostals*** ↔ *Self limited*
- **Myocarditis** : in neonates
  - ♦***Arrythmia*** ↔ *High mortality*
  - ♦***Heart failure***
- **Type I DM**
- **Generalised ds** :in infants
  - ♠ *Heart & liver*
  - ♠ ***Brain***

No antiviral drugs or vaccine

Other enterovirus types

Type 68	Type 70	Type 71
✓ Pneumonia ✓ Bronchitis in children	➢ Acute hgic conjunctivitis	❖ Aseptic meningitis & encephalitis. ❖ Paralysis

Laboratory diagnosis

	Polioviruses	Coxsakieviruses	ECHO Viruses
A-Specimen	**1-Throat swab** : early **2-Stools** :late **3-CSF** : in meningitis		
B-Direct demonstration of virus	**RT-PCR** : detects RNA ↓ Rapid diagnosis of ***meningitis***		
C-Isolation of virus	**On MKTC** → CPE ✓ *Serotyping by Nt* : addition of monoclonal Abs		
D-Serology: Nt	**Rising** titer of **IgG 4** folds in 2 samples		
		Not reliable due to ***multiplicity of Ags***	

Viral gastroenteritis

DNA	*RNA*			
♦ **Adeno**viruses type **40&41**	♦ **Rota** viruses ♦ **Corona** viruses	♦ **ECHO** viruses ♦ **Coxsakie** viruses	♦ **Calici** viruses e.g Norwalk virus	♦ **Astro**viruses

Rota viruses

Family: REO (respiratory enteric orphan)

Structure

1-Genome	2-Capsid	Envelope	Serotypes
• DS RNA –ve sense • Segmented	⋆Double layered ⋆Wheel shape	Non enveloped	5 serotypes cause human ds

Mode of transmission

Feco oral & contact with contaminated surfaces ⟷ *Nosocomial infection*

Pathogenesis

1ry replication occurs in villi of small intestine

↓ reabsorption of glucose & Na+

Virus is excreted in large amounts in stools for 2-12 days

Cl. P

Most common cause of ***infantile*** gastroenteritis (asymptomatic in adults)

Abdominal pain, vomiting & severe watery diarrhea → Dehydration → death

Immunity

Local immunity (IFNα &sIgA) is more important, but short lived

Reinfections are common

Maternal Abs protect infant in 1st ms

Treatment : Fluid & electrolyte replacement

Prevention

Waste water sanitation	Live attenuated oral vaccine : Given in early infancy	
most important	***Pentavalent RV5*** Human-bovine reassortants (3 doses)	***Monovalent RV1*** Human type (2 doses)

Laboratory diagnosis

Direct detection : in stools			Serology : ELISA
EM	ELISA	RT-PCR: Detects viral RNA (most sensitive)	Rising Ab titer
Wheel shape	Detects viral *Ag*	*Genotyping* the virus in stools	

Oncogenic Viruses

Viruses that induce **host cell transformation**

I-Characters of transformed cells

- **Change in growth pattern**
  - ↑ growth rate
  - Loss of contact ⊖
- **IC changes**
  - ↑ metabolic rate & glycolysis
  - ***Integration*** of ***viral NA*** into genome
- **Surface changes**
  - ***New*** virus specific ***Ags***
- **Tumorgenecity**
  - Produce tumor in test animal

II - Mechanisms of cell transformation

Tumor DNA & RNA (Retro) viruses generate *DNA provirus (except HCV)*

Integration into cell chromosome

- Introduction of **new transforming gene**: Viral oncogene (v onc)
- Change in expression of **protooncogene**
- Inactivation of **tumor suppressor gene**
  - e.g p53
- Inhibition of **apoptosis**
  - e.g E6 Ag of HPV
  - ⊖ apoptosis of UV rays damaged cells

Types of tumor viruses

Type	Family	Virus	Disease
I-DNA	*A-Herpes*	1-HSV 2	Cancer *cervix*
		2-EBV	♦ *Burkitt* lymphoma ♦*Nasopharyngeal* carcinoma
		3-HHV 8	*Kaposi* sarcoma
	B-Papova	Human papilloma Virus	♣ *Genital* tumor ♣*Laryngeal* papilloma
	C-Hepadna	Hepatitis B	*Hepatocellular* carcinoma
	D-Pox	Molluscum contagiosum	Molluscum contagiosum
II-RNA	*A-Retro*	HTLV-1 Has reverse transcriptase DNA ***provirus*** Integration	Adult *T cell leukemia & Lymphoma*
	B-Flavi	Hepatitis C(***No RT*** or ***provirus***)	*Hepatocellular* carcinoma

Slow viruses & Prions

Disease Characters

Long IP : (ms or yrs) | Affect CNS : Long chronic progressive course | Fatal

I- Conventional viruses

Measles : Subacute **sclerosing panencephalitis**

JC virus : Progressive encephalopathy

II - Prions

A-General Characters

Infectious ***protein*** with ***no nucleic acid***

Highly resistant to
- ♦ UV &γ rays
- ♦ Formaldehyde&ethanol
- ♦ Dry heat & boiling

Sensitive to
- ♠ Household bleach
- ♠ Ethanol (90%)
- ♠ Autoclave (1 hr for 121C)

Guanidine isocyanate
Decontamiante
instruments & supplies

B-Modes of transmission

Ingestion of diseased **brain**

Transplantation of cornea & dura matter from infected donor

Pathogenesis

Aggregation of prion protein (PrP) within neurons → Vacuolation → ***Spongioform*** changes in brain

7

NO → ***Inflammation*** ↔ ***IR***

Diseases

In man
- **Creutzfeldt – Jakob** ds
- **Kuru**

In cattle & sheep
- **Bovine spongioform** encephalopathy (**mad cow**)

Laboratory diagnosis

Brain biopsy: Spongioform changes

No *Serology or Tissue culture*

Prevention

Slaughtering infected animals | Destruction of carcasses | ***No vaccine***

Treatment : ***No antiviral*** drug

Collective topics

Viruses causing RTIs

1-Rhinoviruses.

2-Influenza viruses.

3-Parainfluenza viruses

4-Respiratory syncitial

5-Adeno viruses

6-Echo viruses

7-Coxsackie viruses

8-Corona viruses

Viruses transmitted fecoorally

1-Polio viruses

2-Coxsakie viruses

3-Echo viruses

4-Viruses causing gastroenteritis:

i.Rota viruses

ii.Calici viruses

iii.Astro viruses

iv.Adenoviruses 40&41

Viruses causing enecephalitis

1-Arbo viruses

2-HSV-1

3-Rabies virus

4-Measles virus

5-Rubella virus

6-Varicella Zoster virus

Viruses causing aseptic meningitis

1-Enteroviruses (commonest causes):

i.Polio viruses

ii.Coxsakie viruses

iii.Echo viruses

2-Mumps virus

3-HSV-2

Viruses transmitted by blood

1-HIV ,HTLV.

2-HBV,HCV,HDV.

3-CMV.

4-Parvovirus B-19.

Sexually transmitted viruses

1-HIV ,HTLV.

2-HBV,HCV.

3-CMV.

4-HPV.

5-Molluscum contagiosum virus

6- HSV-2

Vertically transmitted viruses

1-Rubella virus.

2-CMV.

3-HBV,HIV,HTLV.

4-Parvovirus B-19.

5-HSV-2&VZV.

Essay Questions

Hepatitis &AIDS

1-Diagnosis and prevention of hepatitis A.

2-Compare and contrast between Hepatitis A &B virus as regards general measures used in prevention and contents of vaccine for each

3-Enumerate serological markers of HBV infection & mention their significance.

4-Mention specific laboratory tests used in diagnosis of Hepatitis C virus and their significance

(Don't mention liver functions tests or ELISA)

5-Discuss viral structure and laboratory diagnosis of HIV

6-Give reasons :

a.Failure to develop an effective vaccine against HIV

b.Hepatitis C infection ismore dangerous than hepatitis A infection.

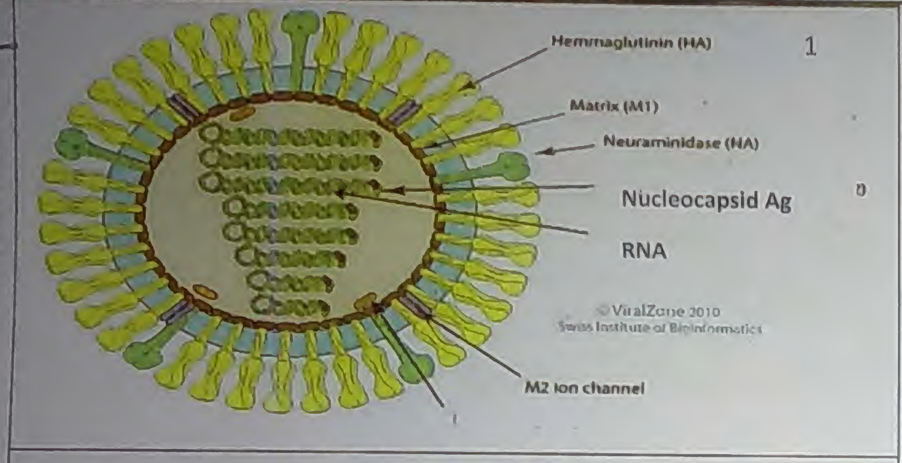
7-Enumerate antiretroviral drugs used in ttt of AIDS.

8-Mention the value of western blot technique in diagnosis of HIV.

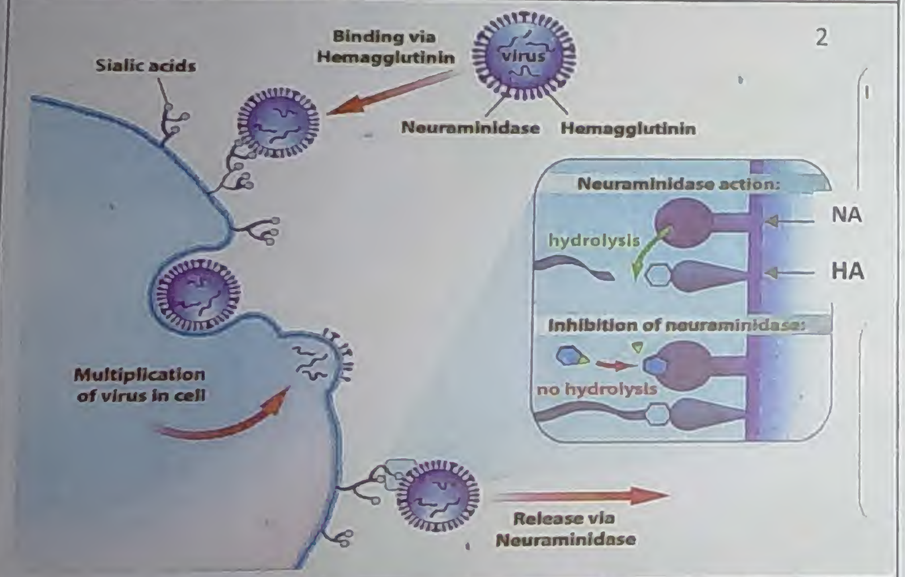
9- Give a short account on novel ttt of hepatitis B

RNA Viruses &oncogenic viruses

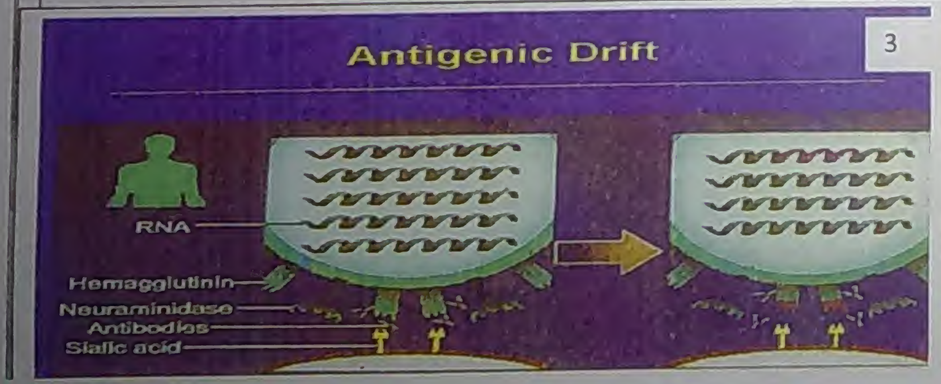
1-Compare and contrast between Orthomyxo and paramyxoviruses as regard genome antigenic variation.
2-Laboratory diagnosis and control of congenital rubella.
3-MMR vaccine.
4-Compare and contrast between CMV & rubella virus infection in pregnancy regarding critical time (CMV :throughout the whole pregnancy) and fetal outcome
5-Influenza chemoprophylaxis.
6-Give reasons : Influenza A virus undergoes antigenic Shift and drift.
7-Mention antigenic drift of influenza virus
8-Give reason : Antigenic shift occurs only in type A influenza virus.
9-Compare and contrast between mode of action of amantadine & acyclovir
10-Influenza viruses are classified into A,B &C serotypes.Explain the basis of this classification and mention 2 differences between between A &B serotypes.
11-Pathogenesis,Cl P & diagnosis of corona virus
12-Laboratory diagnosis of RNA oncogenic viruses.
13 Mechanisms of cell transformation by oncogenic viruses
14-Give an account on human diploid vaccine of rabies.
15-Enumerate 2 arboviruses common in Egypt and their modes of transmission
16 Pathogenesis of viral hgic fevers and mention 3 examples
18-Laboratory diagnosis of rota virus infection
19-Define herd immunity and mention one vaccine that has this property
20-Give reason : a.oral vaccine of polio is contraindicated in a feverish child.
b.Sabin vaccine is preferrable in national preventive programs against poliomyelitis
21Compare and contrast Salk and Sabin vaccine regarding preparation and route of administ.
22-Give reason : a.it is hard to control diseases caused by rhinoviruses (multiple serotypes…….).
b.Human diploid vaccine has replaced crude nervous tissue vaccine in prevention of rabies.
c.Rubella virus causes teratogenic effect only if transmitted during 1st trimester.
23-Mention the causative agent & mode of transmission of : a. German measles b.Rift valley fever. c.Dengue fever.


Hemmaglutinin (HA)
Matrix (M1)
Neuraminidase (HA)
Nucleocapsid Ag
RNA
ViralZone 2010
Swiss Institute of Bioinformatics
M2 ion channel

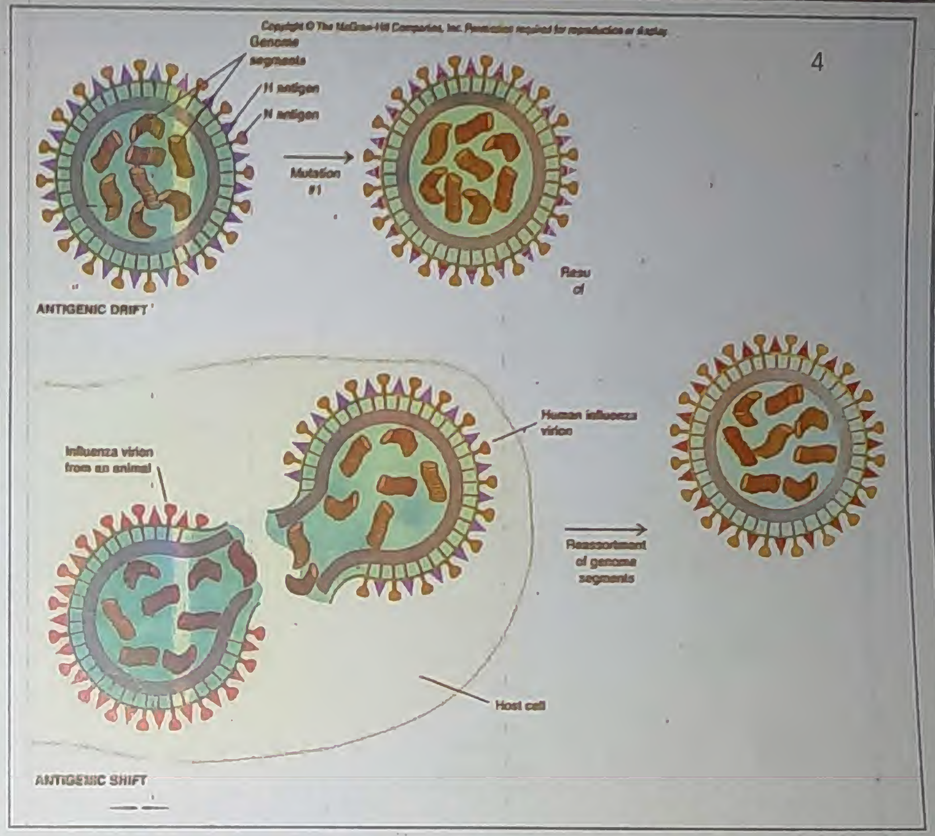
1


Binding via
Hemagglutinin
virus
Sialic acids
Neuraminidase
Hemagglutinin
Neuraminidase action:
NA
hydrolysis
HA
Inhibition of neuraminidase
no hydrolysis
Multiplication
of virus in cell
Release via
Neuraminidase

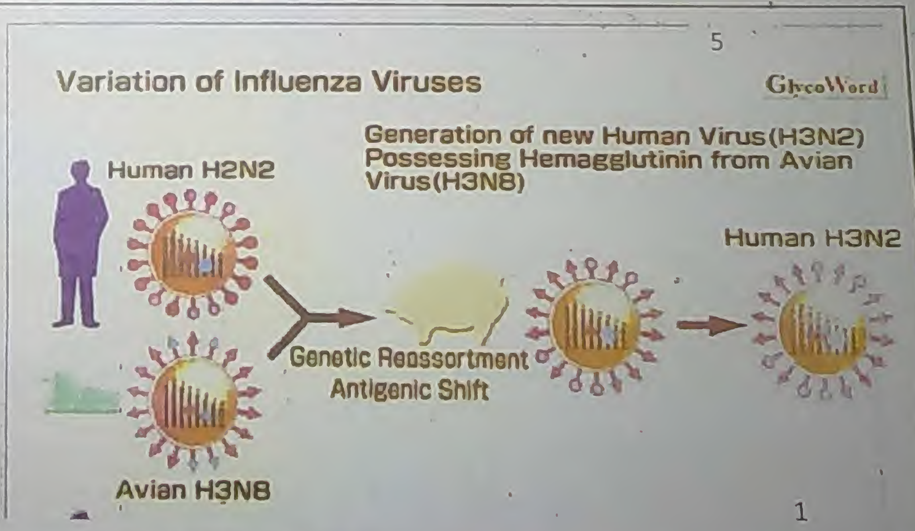
2


Antigenic Drift
RNA
Hemagglutinin
Neuraminidase
Antibodies
Sialic acid

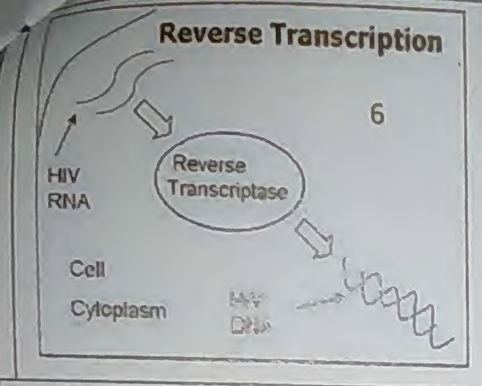
3

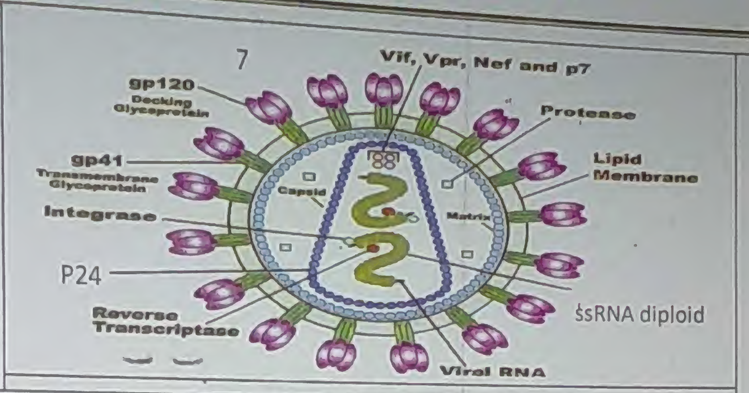

Genome
segments
H antigen
N antigen
Mutation
#1
ANTIGENIC DRIFT
Influenza virion
from an animal
Human influenza
virion
Reassortment
of genome
segments
Host cell
ANTIGENIC SHIFT

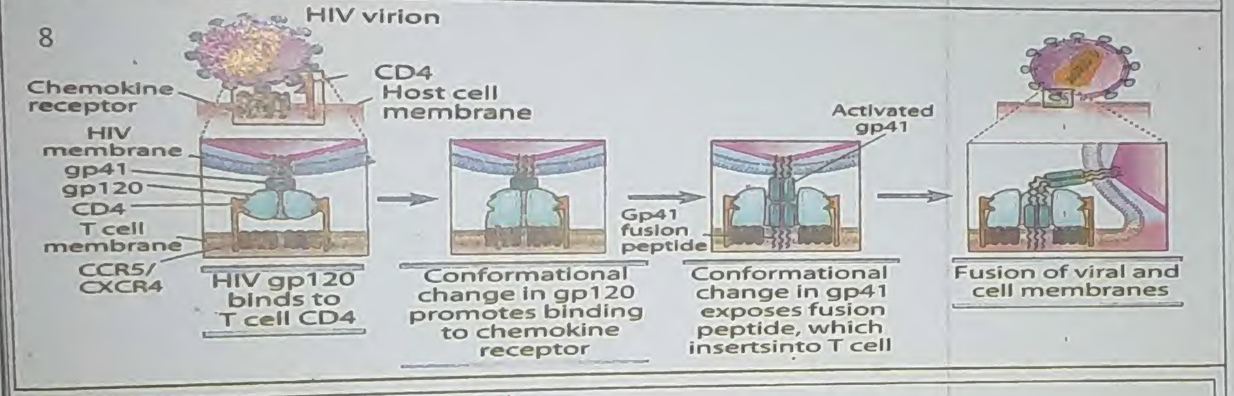
4

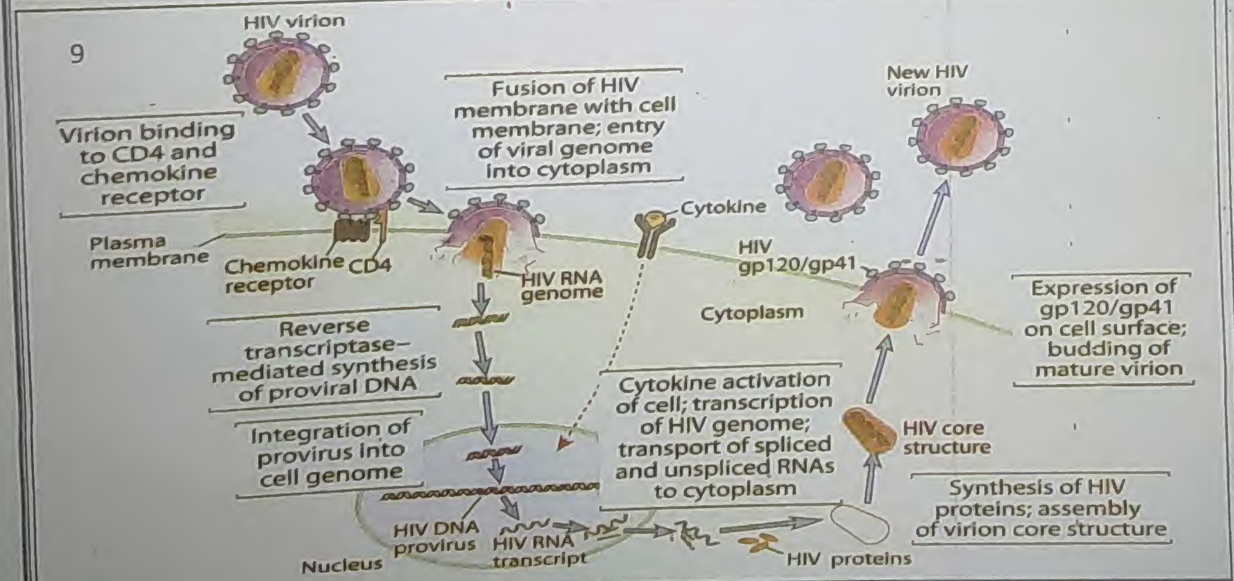

Variation of Influenza Viruses
GlycoWord
Generation of new Human Virus(H3N2)
Possessing Hemagglutinin from Avian
Virus(H3N8)
Human H2N2
Human H3N2
Genetic Reassortment
Antigenic Shift
Avian H3N8

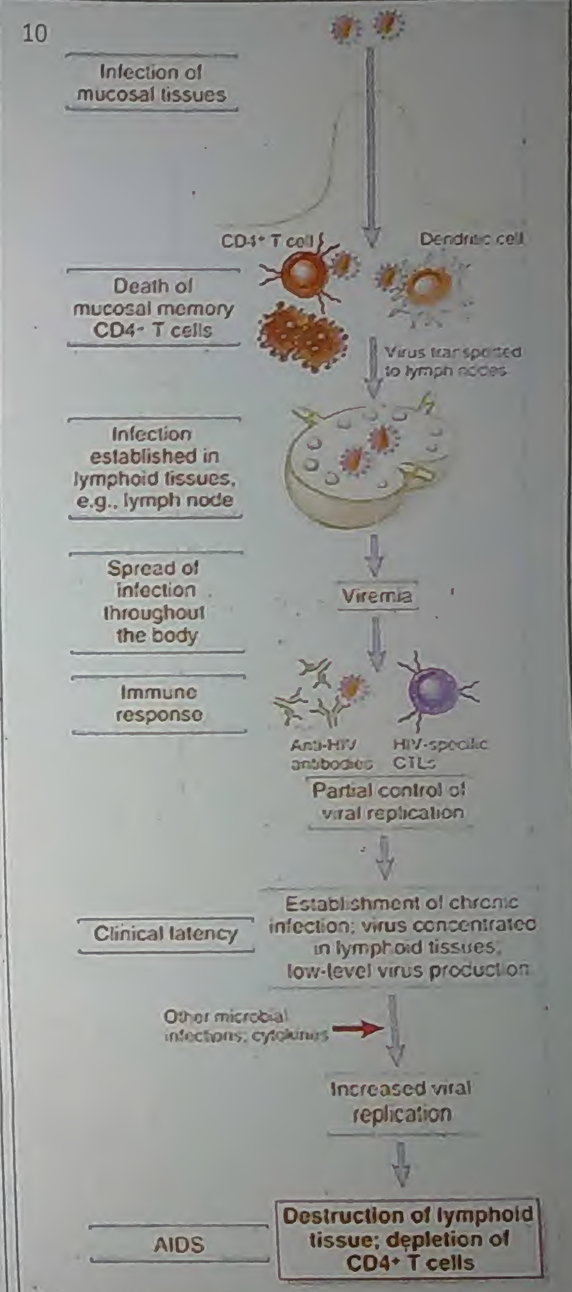
5


Reverse Transcription
6
HIV RNA
Reverse Transcriptase
Cell
Cytoplasm
HIV DNA


7
Vif, Vpr, Nef and p7
gp120
Docking Glycoprotein
Protease
gp41
Transmembrane Glycoprotein
Lipid Membrane
Capsid
Integrase
Matrix
P24
Reverse Transcriptase
ssRNA diploid
Viral RNA


8
HIV virion
Chemokine receptor
CD4
Host cell membrane
HIV membrane
gp41
gp120
CD4
T cell membrane
CCR5/ CXCR4
HIV gp120 binds to T cell CD4
Conformational change in gp120 promotes binding to chemokine receptor
Gp41 fusion peptide
Activated gp41
Conformational change in gp41 exposes fusion peptide, which insertsinto T cell
Fusion of viral and cell membranes


9
HIV virion
Virion binding to CD4 and chemokine receptor
Fusion of HIV membrane with cell membrane; entry of viral genome into cytoplasm
New HIV virion
Cytokine
Plasma membrane
Chemokine receptor
CD4
HIV RNA genome
HIV gp120/gp41
Cytoplasm
Expression of gp120/gp41 on cell surface; budding of mature virion
Reverse transcriptase–mediated synthesis of proviral DNA
Integration of provirus into cell genome
Cytokine activation of cell; transcription of HIV genome; transport of spliced and unspliced RNAs to cytoplasm
HIV core structure
Synthesis of HIV proteins; assembly of virion core structure
HIV DNA provirus
HIV RNA transcript
Nucleus
HIV proteins


10
Infection of mucosal tissues
CD4+ T cell
Dendritic cell
Death of mucosal memory CD4+ T cells
Virus transported to lymph nodes
Infection established in lymphoid tissues, e.g., lymph node
Spread of infection throughout the body
Viremia
Immune response
Anti-HIV antibodies
HIV-specific CTLs
Partial control of viral replication
Clinical latency
Establishment of chronic infection; virus concentrated in lymphoid tissues, low-level virus production
Other microbial infections; cytokines
Increased viral replication
AIDS
Destruction of lymphoid tissue; depletion of CD4+ T cells